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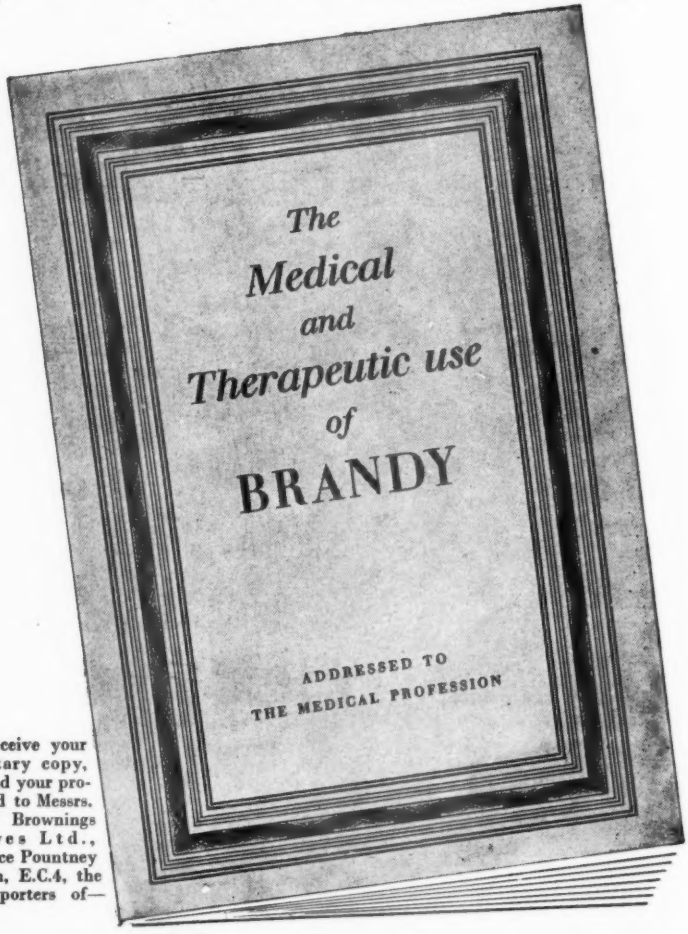

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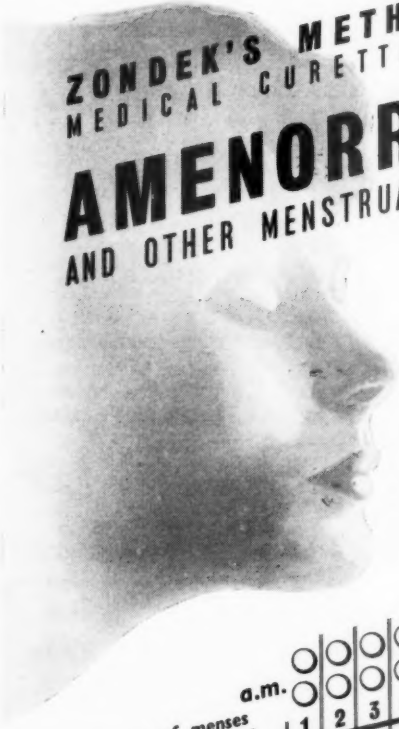

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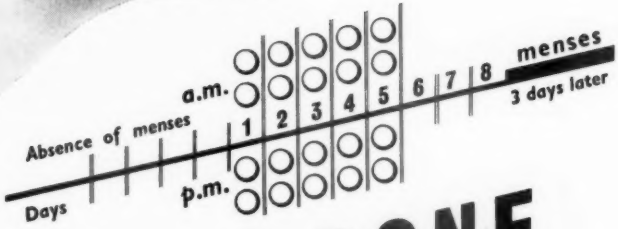

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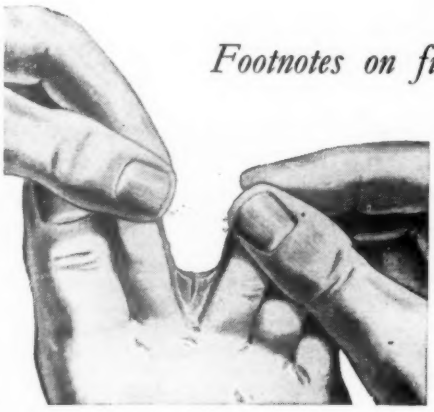

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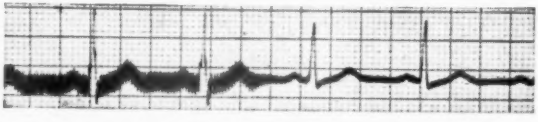

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Section of Neurology

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[*April* 1, 1954]

MEETING AT THE WEST END HOSPITAL FOR NERVOUS DISEASES, LONDON

Charcot's Vertebral Osteoarthropathy.—C. WORSTER-DROUGHT, M.D.

W. P., aged 48, a Pole, was first seen in September 1947, complaining of occasional "faintness" of three weeks' duration and unsteadiness of gait in the dark for the past three years.

He had lost his right eye in the first World War, but the left eye showed an Argyll Robertson pupil. The knee and ankle jerks were absent; there was some inco-ordination of his lower limbs with positive Romberg's sign, tendo Achillis analgesia and diminished vibration sense in the legs. The W.R. was negative in blood and cerebrospinal fluid, the latter showing normal cells, 35 mg.% total protein and a Lange curve of mild "paretic" type.

He made no complaint of his back, but on examination showed a pronounced scoliosis in the lumbar region with convexity to the right and some hollowing over the first and second lumbar vertebræ. Movements of forward and lateral flexion of the spine were practically full but there was some limitation of backward extension. The patient had been aware of the spinal deformity for only two months and he had noticed neither pain nor stiffness in the back.

There was no history of trauma, and the only change of circumstances that might have had any bearing on the condition was that for the past few months his work had entailed the lifting of heavy furniture. Owing to the spinal deformity, lumbar puncture was possible only between the fifth lumbar vertebra and first sacral segment.

X-ray examination of the spine showed destructive changes of the adjacent surfaces of the bodies of the first, second and third lumbar vertebræ with subluxation of the latter two vertebræ. In addition, there was some lateral hyperplasia with newly-formed bone both anteriorly and laterally. In the lateral view the second and third lumbar vertebræ overlap, giving the appearance of fusion, while some soft hyperplastic bone is seen in the anterior portions of these vertebræ.

In the thoracic region (lateral view) osteoarthritis in the form of osteophytic formation is seen at the anterior margins of the vertebræ.

His condition has remained unchanged for the past six and a half years, and he continues to work satisfactorily.

Myotonia Acquisita.—C. WORSTER-DROUGHT, M.D.

Mrs. W. A., aged 28, first seen on 11.11.48, complaining of inability to walk without assistance owing to stiffness of the legs, and difficulty in speaking as "her tongue seems in the way".

History.—One morning in May 1948 she awakened with severe tingling sensations in the hands and feet; these symptoms persisted, and after about a week were followed by weakness of the hands, arms and legs. Her legs then appeared to "become stiff", especially below the knees, and by the end of the following month (June 1948) she was unable to walk, although the tingling sensations had disappeared.

No previous history of noteworthy illnesses excepting that for about three years she had had a rather large "gland" on the right side of her neck.

Family history.—Nil relevant.

Physical examination (11.11.48).—She could not walk alone but could do so when supported on each side; even then her gait was awkward, with stiffened legs and feet firmly plantar-flexed, toes pointing downwards and adductor scissor spasm.

She showed slight left-sided ptosis, but the other cranial nerves normal. No temporal or malar hollowing; no baldness and no cataract. Speech slow, much slurred and indistinct. Reactive myotonia in tongue, which was protruded only slowly. Sternomastoids thin but strong.

Radial jerks, knee and ankle jerks absent. Abdominal reflexes present but sluggish; plantar responses flexor.

The arms were mobile but nearly all muscles showed both active and reactive myotonia, which was especially pronounced in the flexors of the wrist, fingers and thumb. Active myotonia present in all the muscles of the legs and in the erector spinæ, while reactive myotonia could be demonstrated in most of the accessible muscles. The active myotonia of the legs and spinal muscles was responsible for her difficulty in walking.

A myotonic reaction was observed in all affected muscles on faradic stimulation, while electromyography showed typical "dive-bomber" myotonic reactions.

Other systems were normal. An electrocardiogram and X-ray examination of the chest gave normal results.

Subsequent progress.—The "gland" in the right side of the neck, when removed (14.3.49), proved to be a benign carotid body tumour wedged into the bifurcation of the common carotid artery and grooved by the external and internal carotid arteries. In order to remove the tumour, the right hypoglossal and spinal accessory nerves had to be sacrificed, with resulting hemiatrophy of the tongue and paresis of the sternomastoid and upper portion of trapezius.

Blood examinations.—Serum potassium 20·1 mg.%, calcium 11·4 mg.%; E.S.R. and blood counts all within normal limits. Urinary creatinine within normal range (1·5 grammes *per diem*) but creatine slightly in excess (0·3 gramme *per diem*).

On quinine hydrochloride 5 grains t.d.s., the patient showed definite improvement in the myotonia after two weeks and even more so when Tab. Diparcol (each tablet of 0·025 gramme), two tablets t.d.s. was added. By April 1949 she was walking without assistance, but still with considerable difficulty in starting.

The patient has continued to improve. A lessened degree of both active and reactive myotonia can still be demonstrated in several of the previously affected muscles, especially on flexion of the wrist and fingers, but no muscular atrophy has developed. The arm, knee and ankle jerks remain absent. She continues under treatment with quinine and Diparcol.

Comment.—Myotonia acquisita occurs sporadically with a fairly acute onset, usually following some infective illness with which a polyneuritis, mild or otherwise, may have been associated. Unlike dystrophia myotonica, muscular atrophy and trophic changes do not occur, nor is there a family history of the disorder. Males are more frequently affected than females.

In the case demonstrated, the early paræsthesia of the extremities followed by muscular weakness suggests some degree of polyneuritis or peripheral neuropathy.

It may be emphasized that myotonia is not a disease *sui generis* but a symptom which may occur in several maladies. In addition to dystrophia myotonica and myotonia acquisita, myotonia also occurs occasionally in severe polyneuritis, Charcot-Marie-Tooth peroneal dystrophy and myxœdema.

Two Cases of Trigeminal Neuropathy.—T. ROWLAND HILL, M.D.

I.—W. S., male, aged 33.

In October 1950 he began to experience "pins and needles" around the right eye. This continued for three months, by which time he realized that the whole of the right side of the face had become numb including the inside of his mouth on the right side.

When seen in December 1950 he had a severe degree of hypalgesia affecting the whole of the right trigeminal distribution, with loss of corneal sensation and reflex. There was severe impairment of light touch sensation over the whole right trigeminal area, but deep pressure sensation appeared normal and equal on both sides of the face.

There was hypalgesia of the anterior two-thirds of the right side of the tongue with loss of taste over this area.

There was no complaint of weakness of chewing but there was deviation of the mandible to the right on opening the mouth and slight right-sided masseter wasting. There was no obvious wasting of the temporal muscle.

There has been no trigeminal neuralgia and herpetic eruption. His main symptom was that the whole of the right side of the face felt as though "it was covered with sticking plaster".

His condition has remained stationary since December 1950. There has been no evidence of any neurological lesion other than that of the right V nerve.

II.—E. S., male, aged 40.

In November 1950 there was a gradual onset of numbness of the lower part of the left side of the face (over the area of the left mandibular division of the trigeminal nerve). It began with a sensation of "thickness" of the left lower lip which slowly spread downwards to the tip of the chin on the left side and then steadily upwards towards the left ear. He noticed numbness inside the left lower lip and also of the left side of his tongue. At the onset there was some paræsthesia over the numb area in the form of "hot and flushed feelings". These lasted for not more than one week. He noticed some weakness of the mandible which recovered after three to four weeks. He also noticed loss of taste on the left side of the tongue for a while at the beginning and also dryness of the mouth on the left side but found both these symptoms improving soon. Otherwise, his symptoms have remained stationary since.

There is hypalgesia and diminution of touch and thermal sensibility over the left mandibular distribution of the V nerve, most marked anteriorly.

There have been no symptoms or signs of any other neurological lesions. His general condition is good and there was no evidence discoverable of any local dental or other infection.

X-ray of skull, sinuses and teeth negative.

Blood W.R. and Kahn negative.

There is still total loss of taste on left anterior two-thirds of tongue.

Comment.—12 cases of this condition have been collected during the last few years. It affects men and women equally, appears in most instances to have no local infectious cause, is commonly progressive for a time, may later recede but usually leaves behind it chronic sequelæ in the form of sensory, motor, sympathetic or parasympathetic palsies or combinations of all these (*see* Figs. 1, 2 and 3).

FIG. 1.—Right-sided motor palsy.

FIG. 2.—Same as Fig. 1 showing right-sided Horner's syndrome.

FIG. 3.—Left-sided motor palsy.

The clinical picture is one of peripheral neuropathy distal to the gasserian ganglion involving part or whole of the sensory fibres and commonly producing motor palsy as well. A unique sign is peripheral sympathetic palsy of the eye with Horner's syndrome, present in most cases and characterizing when present, the most chronic of all the changes.

Several cases followed up over a number of years have shown Horner's syndrome unchanged whilst all else has remitted. The presence of Horner's syndrome together with corneal analgesia indicates very distal neuropathic changes, distal to the ciliary ganglia. So also does the parasympathetic loss of taste over the anterior two-thirds of the tongue which is commonly found in these cases combined with analgesia of the tongue—the neuropathy being thus distal to where the chorda tympani joins the lingual nerve.

Some cases show unilateral dryness of the mouth from distal salivary paralysis. Paræsthesia rather than pain is characteristic. The ætiology is obscure.

Papilloma of Choroid Plexus.—GEOFFREY KNIGHT, F.R.C.S.

Female, aged 19. Admitted 26.1.54 on account of headache and vomiting of six months' duration with unsteady gait, double vision and squint of fourteen days' duration.

The patient had been perfectly well until six months previously when she woke up one morning and was violently sick. Three weeks later she had a further attack of projectile vomiting without associated nausea, occurring at night. This time she developed severe bilateral headache which lasted for one hour. Similar attacks of headache and vomiting occurred at intervals of ten to fourteen days up to the time of her admission. They only occurred at night or on waking in the morning. For fourteen days she had tended to stumble and lose her balance when walking and had developed diplopia and a convergent squint in the left eye.

Examination revealed evidence of mental confusion, marked bilateral papillœdema—greater on the right. V.A.L. 6/12. V.A.R. 6/18. Visual fields full. Pupils normal. Left VI nerve weakness with diplopia on looking to the left. Coarse nystagmus to right and transient nystagmus to left. Corneal

reflexes normal, no facial weakness. Hearing normal. Phonation slow. Swallowing and palate movements normal. Power and sensation normal in all limbs. Right-sided reflexes somewhat less than left-sided. Right plantar reflex extensor from outer border of foot. Hypotonus in both upper limbs with dysdiadokokinesia in left hand more than right. No intention tremor but static tremor in both hands.

Ventriculography revealed marked internal hydrocephalus with dilatation of the aqueduct. The fourth ventricle was pushed upwards and towards the left by a space-occupying lesion which was on the right side.

Craniotomy.—A suboccipital craniectomy was performed removing the occipital plates and arch of the atlas. The dura was under great tension. It was divided in a T-shaped manner. The right cerebellar tonsil was very prominent and thickened to four times its normal size and displaced downwards into the foramen magnum. In order to disimpact this pressure cone the right tonsil and lower third of the right cerebellar hemisphere were amputated. On elevating the remainder of the hemisphere the margin of tumour was visible lying beside the brain-stem and projecting upwards into the right hemisphere. This tumour was soft and with surface appearances suggestive of medulloblastoma. A small portion was taken for microscopic examination with a view to deep X-ray therapy. Post-operative recovery uneventful. The left VI nerve weakness recovered. Nystagmus persisted. Papillœdema decreased, but the patient remained mentally confused with occasional drowsiness or aggressiveness.

Pathological section reported as papilloma of the choroid plexus.

23.2.54: A further operation was performed for excision of papilloma of the choroid plexus. With the patient in a sitting position the original wound was reopened. On opening the dura there was no evidence of raised intracranial pressure. The cerebellar hemispheres were pulsating normally. On elevating the amputated right cerebellar hemisphere a plum-coloured tumour mass was seen completely replacing the anterior two-thirds of the hemisphere as far laterally as the right lateral wall of the posterior fossa. The posterior inferior cerebellar artery was stretched over this mass and the anterior inferior cerebellar artery was stretched over its anterior surface. The lateral two-thirds of the tumour were now amputated in order to gain space. The tumour was then drawn gently laterally. The mesial border of the tumour was seen to occupy a greatly distended fourth ventricle, leaving an aperture a few millimetres wide on its left inner margin for the downflow of cerebrospinal fluid. It was possible to rotate the tumour out of the fourth ventricle and finally to divide its vascular attachments to the choroid plexus and remove it.

Post-operative recovery uneventful.

Gastrocystoma of Spinal Cord.—GEOFFREY KNIGHT, F.R.C.S.

Mr. Geoffrey Knight also showed a case of congenital gastrocystoma occupying an intramedullary position in the lower cervical and upper dorsal cord of a child aged 15 months, which had been removed by laminectomy. A detailed account of this case will appear in the *British Journal of Surgery* (1955).

Focal Epilepsy with Calcifying Intracranial Tuberculoma After Recovery from Tuberculous Meningitis.—JOHN LORBER, M.D., M.R.C.P.

P. T., male, born on 9.7.44. Aged 9¼ years.

History.—October 1949, gross cervical lymphadenopathy with fever.

22.11.49: Admitted to Surgical Unit, Sheffield Children's Hospital. High fever. Positive tuberculin. No improvement on penicillin and Sulphamezathine.

2.12.49: Headache. Minimal neck stiffness. First seen next day. Early choroidal tubercle at 2 o'clock near the disc margin of right fundus. X-ray chest: probably miliary tuberculosis. C.S.F. characteristic of tuberculous meningitis. Tubercle bacilli recovered. X-ray skull negative.

Treatment of tuberculous meningitis with intramuscular and intrathecal streptomycin between December 1949 and June 1950. During treatment developed a temporary spinal block, but three AEGs were normal. Good clinical progress, apart from right-sided convulsions three weeks and six months after admission, without deterioration in C.S.F. C.S.F. became normal eight months after beginning of treatment.

Further progress was uneventful except for fits. The first slight fit after his recovery occurred in April 1952 and 3 more definite fits in August 1952. EEG: "The record consists of a wide range of frequencies and is dysrhythmic. There is a dominant rhythm of 9 c/s with irregular moderate to high amplitude theta waves of 4–5 c/s interspersed in all areas. The slow activity is frequent and of high amplitude in the left hemisphere, particularly in the temporo-parietal region." X-ray skull: nil definite, possibly early intracranial calcification. C.S.F. normal. Anticonvulsant therapy started. Gradually increasing doses because of recurrent fits at irregular intervals up to January 1954. Fits now very slight. Receiving phenobarbitone 1 grain daily and phenytoin 2¼ grains daily.

Intracranial calcification became definite in January 1953 and has increased in density since. Stereoscopic views suggest that the calcifications are situated about ½ in. to the left of the mid-line and about 2 in. above the floor of the posterior fossa. They are approximately at the junction of the posterior and middle fossæ and spacially probably lie to the left of the posterior part of the aqueduct of Sylvius (Fig. 1).

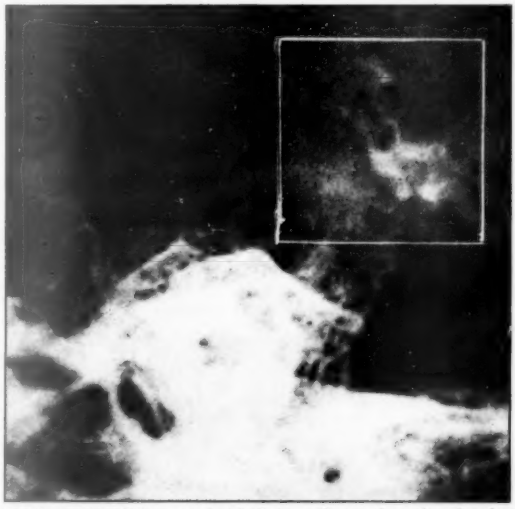

FIG. 1.—Radiograph of the area behind the sella turcica, showing intracranial calcification.

Present condition excellent. Hearing good. I.Q. 118 (Terman-Merrill). Attends ordinary school. No behaviour problems. Healed choroidal tubercle persists.

Comment.—Intracranial calcifications commonly develop between two and four years after the onset of tuberculous meningitis and may be discovered radiologically in about two-thirds of the cases. In the majority the calcifications occur at the site of the basal exudate and may be extensive. Less often the calcifications appear to be intracerebral. As a rule neither type causes any symptoms (Lorber, J., 1952, *Arch. Dis. Childh.*, **27**, 542). In this patient, however, a large calcifying intracerebral tuberculoma in the left temporal region is associated with fits and with EEG changes of epilepsy in the same area. It is probable that the tuberculoma is the epileptogenic focus, but it does not appear to cause any other signs or symptoms.

Mr. Ian R. McCaul was asked for his opinion as a neurosurgeon on the part that surgery had to play in the treatment of calcified tuberculomata. In reply, he gave it as his opinion that surgery had no place in the treatment of such a lesion but that occasionally non-calcifying tuberculomata did require removal because of their expanding nature.

? Acute Bilateral Brachial Radiculitis (Neuralgic Amyotrophy).—E. C. O. JEWESBURY, D.M., M.R.C.P.

J. B., aged 60. Hospital porter.

History.—January 1953. Abdominal pain and anæmia (Hb 50%) believed to be due to bleeding duodenal ulcer. Benzidine test of stools was weakly positive and barium meal showed a badly filling duodenal cap. C.N.S. apparently normal. Was six weeks in Highlands Hospital (Dr. J. Sharkey) and improved rapidly with post-ulcer diet and iron (Tab. Fersolate). 16.3.53: Returned to work symptomless; Hb 84% rising to 105% six weeks later. Within a week of returning to work he began to have pain in back of neck, radiating into both shoulders and upper arms. The muscles of the shoulders were tender for a few days. Two to three weeks after the onset of pain he noticed weakness in raising right arm. Shortly afterwards the left shoulder movements also became affected, though the right remained the worse. No history of infection, injury or inoculations.

Examination.—When first seen in July 1953, he still had aching pains in neck and upper limbs and there was marked wasting and weakness in the distribution of C. 5–6 segments, especially the right side. Coarse fasciculation of shoulder and pectoral muscles. No wasting or weakness of hands. Neck movements full. Power of lower limbs normal. No sensory loss anywhere. Arm reflexes absent, knee jerks brisk, ankle jerks present (left slightly brisker than right). Plantars: left doubtful, right flexor.

Progress.—Has been seen again November and December 1953 and February 1954 and has been treated by abduction splints and physiotherapy but aching has persisted, fasciculation remains and weakness has become more pronounced and has spread. He has slight discomfort in neck on turning head, but this does not radiate. Has intermittent dull ache from shoulders to hands, especially in little fingers recently. Has complete paralysis of both shoulder girdles (Fig. 1). Dorsiflexion of wrists now weak and some recent wasting and weakness of small muscles of hands. Sensation normal. No paræsthesiæ. Says legs jump in bed at night (left more than right). Gait normal. Micturition normal. Reflexes now:

FIG. 1.—J. B., April 1954, showing wasting of shoulder muscles.

	R.		L.
Upper limbs	0		0
Abdomen	0		0
	0		0
Knee jerks	0		+
Ankle jerks	(+)	<	(+)
Plantars	↓		↓

Investigations.—Plain X-rays of cervical spine and chest were normal. Blood W.R. negative. Hb. 84%. C.S.F.—Blood-stained (traumatic). Pressure 155 mm. Queckenstedt: Free rise and fall. Clear supernatant fluid. R.B.C. present. Protein 120 mg./100 ml.

Electromyography.—November 1953: Showed fibrillation at rest and discrete motor unit activity on voluntary contraction of left deltoid and biceps. The discrete potentials were disintegrated and of short duration. "Nothing in support of a motor neurone disease and findings are more in keeping with a distal neuronitis."

E.M.G. December 1953: Injection of Tensilon produced gross fasciculation in muscles of both shoulders and upper limbs. In the deltoid there was no motor unit activity on volition, while in the biceps only discrete motor unit activity could be detected. These findings were regarded as in keeping with a distal neuronitis, though discrete motor unit activity and clinical deterioration now cast some doubt.

Dr. P. Bauwens: *Electro-diagnostic Investigations.*

I first saw this patient on 17.11.53 and found as follows:

(*a*) On stimulation of the upper trunk of the brachial plexus on the left side, only very weak diffuse responses were obtained in the deltoid and biceps.

(*b*) Direct stimulation of these muscles with currents of long duration (galvanic) elicited sluggish responses, while the ratio of the thresholds for long and short duration stimuli pointed to gross denervation.

(*c*) Electromyographic exploration of these muscles revealed fibrillation at rest, while on volition a grossly reduced motor unit activity pattern, composed of low amplitude potentials of short duration, was obtained.

At a subsequent examination of the patient a month later, I found much the same situation in the biceps, but was unable to detect any motor unit activity on volition in the deltoid. An intravenous injection of 15 mg. of Tensilon, which is a short-acting, anti-curare drug with Prostigmin-like effects, provoked gross fasciculation.

These findings are in contrast with those encountered in myelopathies, whether due to motor neurone disease or cervical spondylosis. In my experience these are characterized by:

(*a*) Moderately good muscle responses to stimulation of nerve trunks: out of keeping with the muscle weakness on volition.

(*b*) Minimal departures from the normal muscle reactions to stimulation with currents of long and short duration.

(*c*) Reduction of electromyographic tracings to a pattern made up of discrete potentials of large amplitude.

(*d*) Fasciculation does not appear to be greatly influenced by an injection of Tensilon.

In myelopathic conditions whole motor units drop out of action as the disease progresses. The disintegrated electromyographic pattern on volition in this particular case suggests that degeneration of the terminal portion of the axon ramifications occurred and inactivated a large proportion of muscle fibres within the motor units.

To recapitulate, this case presents electrodiagnostic signs of grossly impaired nerve conduction or neuromuscular transmission, coupled with signs of extensive denervation of the muscles. Furthermore, electromyographic exploration suggests that this denervation is diffuse in that it affects individual muscle fibres as distinct from whole motor units.

Without prejudice to the history and clinical picture, I would, on electrodiagnostic evidence, put this patient in the category of polyneuritis.

Intracranial Aneurysm of Left Internal Carotid Artery.—JOSEPH MINTON, F.R.C.S.

Male, aged 56. Insurance agent.

On admission to the Hampstead General Hospital complained of severe pain round left eye of ten days' duration, with drooping of left eyelid for four days.

History.—Slight twinges of pain round left eye for two years.

Past history.—Gross impairment of vision in left eye since age of 5 years. Pain in distribution of left trigeminal nerve thirty years ago, lasting two weeks. Headaches: very occasionally all his life.

On examination.—Healthy-looking man. C.V.S.: apparently normal. B.P. 130/90. R.S., abdomen and general examination, n.a.d. C.N.S., no neck stiffness. Arms and legs normal.

Abnormal findings.—II nerve: Vision, right 6/12; left, appreciates light only.

Left eye: III nerve: Complete palsy on left; fixed dilated pupil; marked ptosis. Paralysis of internal rectus, superior rectus, inferior rectus and inferior oblique. IV nerve: Weakness of superior oblique. VI nerve: Weakness of external rectus. V nerve: All sensations normal.

No abnormal findings in any other cranial nerves.

Investigations.—Hb 104%, W.B.C. 4,000. E.S.R. 2 mm. in the first hour. Chest X-ray: normal. W.R. and Kahn negative. Skull X-rays normal. Left carotid arteriogram at the National Hospital for Nervous Diseases: aneurysm of left internal carotid artery (Fig. 1).

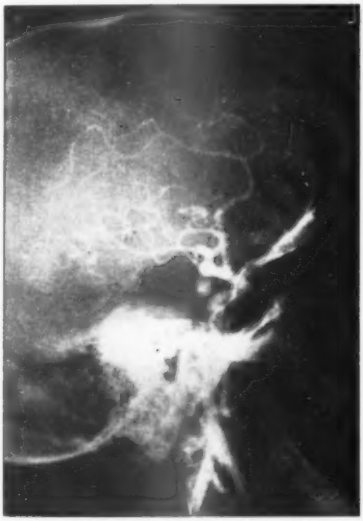

FIG. 1.—Arteriogram shows intracranial aneurysm of the left internal carotid artery.

FIG. 2.—Post-mortem appearance: a ruptured aneurysm of the left internal carotid.

Progress.—After one week, signs of recovery in the paralysed nerves.

Readmission.—Eye signs: left complete ptosis. Left III, IV, VI nerve palsy. Moderately severe headache in left supra-orbital region radiating to left occipital region. No neck stiffness.

Third day after admission, complained of very severe headache. Became unconscious and had convulsions. Died four hours later.

Summary of post-mortem findings (Dr. G. F. Bacon).— Brain: A considerable quantity of blood clot was seen in the subarachnoid space. The origin was a ruptured aneurysm of the left internal carotid. This aneurysm was situated under the III nerve which was stretched and flattened over it and was, therefore, subdural and there was a rent in its lateral surface. There was also an intradural leak and blood clot surrounded the IV and VI nerves as they lay in the wall of the cavernous sinus and had extended to envelop the trigeminal ganglion (Fig. 2).

A portion of the junction between the aneurysm and the internal carotid artery itself was taken for section which, however, revealed no microscopical abnormality. The muscular layer was not degenerated, the elastin not hypertrophied, nor was there any cellular infiltration.

I am grateful to Dr. M. Kremer for his help in the investigation of this case.

Myasthenia Gravis at the Age of 11 Years.—JOSEPH MINTON, F.R.C.S.

Female, aged 11 years 9 months.

Attended at the Queen Elizabeth Hospital for Children on 5.1.50 complaining of drooping of the right upper lid for two weeks. She also complained of occasional double vision.

Past history.—No previous illnesses or injury.

On examination.—(Fig. 1) Complete ptosis of the right upper lid and a weakness of the left sup. rectus and the left inf. oblique. V. 6/6 each eye. Fundi normal. Heart, lungs and C.N.S. normal. Face immobile. Right side of face was flatter than the left side. C.S.F. normal. X-ray skull normal. X-ray chest no enlargement of the thymus gland.

She was given an injection of Prostigmin (3 mg.). Fifteen minutes after the injection the ptosis of the right upper lid disappeared (Fig. 2). She was treated as an in-patient for two weeks: Prostigmin

FIG. 1.—Myasthenia gravis, showing the condition on 7.2.50; ptosis of the right upper lid.

FIG. 2.—The same patient fifteen minutes after a Prostigmin injection (3 mg.).

FIG. 3.—The same patient in August 1953. All treatment was stopped in 1952.

injections (3 mg.) were given at six-hourly intervals. The injections were gradually replaced by giving Prostigmin tablets (30 mg.).

Progress.—She continued taking Prostigmin tablets (30 mg.) at six-hourly intervals. On 16.3.50 she reported at the Out-Patient Department with ptosis of the left upper lid. The right upper lid was in normal position. Prostigmin injections (3 mg.) were again started. Her condition was stabilized with two Prostigmin injections (3 mg.) daily and Prostigmin tablets (30 mg.) every three hours.

In September the Prostigmin injections were not necessary. The Prostigmin tablets four-hourly controlled the ptosis of both lids. In January 1951 the tablets (30 mg.) were only given six-hourly. In the course of 1951 the number of tablets was gradually reduced, and in 1952 she stopped taking Prostigmin. The ptosis of the lids never returned, but she had a permanent weakness of the left superior rectus muscle of the eye. She only saw double when looking up and to the left. There are now no symptoms and treatment has been stopped. General physical and endocrine development is perfectly normal.

The girl, now 16 (Fig. 3), is still attending school and taking part in all outdoor activities.

I am grateful to Mr. J. S. Sheppard (Photographic Department of the Royal Free Hospital) for his help with the illustrations.

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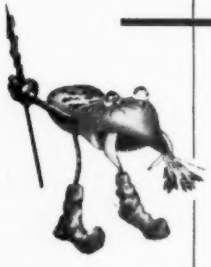

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Section of Odontology

President—ARTHUR BULLEID, F.D.S., L.R.C.P., M.R.C.S.

[*March* 20, 1954]

COMBINED MEETING WITH THE ODONTOLOGICAL SECTION OF THE BIRMINGHAM MEDICAL INSTITUTE AT THE MOUNT VERNON CENTRE FOR PLASTIC AND JAW SURGERY, MOUNT VERNON HOSPITAL, NORTHWOOD, MIDDLESEX

Three Cases.—R. L. G. DAWSON, F.R.C.S.

Case I.—Male, aged 70.

A recurrent rodent ulcer of the upper lip and nose, wide excision nose, total excision upper lip. Tubed pedicle reconstruction of nose and upper lip.

Case II.—Male, aged 42.

A severe compound injury to left face, with stove-in malar bone, and ethmoids. The right eye had been blind for many years, and the floor of the left orbit was grossly displaced. Primary repair and subsequent nasal infracture had attained a satisfactory nose, but he needed a dacryocystorhinostomy. It was proposed to accept the displaced position of the left globe as manipulations to improve its position would be an unjustifiable risk to the sight of this, the only functioning eye.

Case III.—Male, aged 11.

A history of gradually enlarging face over the last one and a half years. Confined to the lower part of the face. No family history of cystic jaw. Intelligence appeared slightly subnormal. Examination revealed bilateral lobular swellings of the mandible, solid and cystic. One swelling transilluminated. Radiographs revealed a bilateral cystic mandible, an irregular area of decalcification in the skull, and a cyst of the upper end of the fibula.

Blood chemistry.—Calcium 9·6 mg.%; phosphorus 6·4 mg.%; alkaline phosphatase 18·1 K.A. units.

Diagnosis.—Polyostotic fibrous dysplasia.

Tumours of Maxilla and Mandible: Three Cases.—RAINSFORD MOWLEM, F.R.C.S.

When surgical removal of a tumour of the maxilla or mandible is indicated much can be done to minimize discomfort, to reduce stay in hospital and to preserve function and appearance by combining the resection and the repair. Before such a procedure is practicable it must be known that the resection can be made adequate to ensure complete elimination of all pathological tissues and that the residual defect will be free from real or potential infection.

Maxillary resections are usually camouflaged by prosthetic supports, which are not applicable until epithelialization is complete. This can be hastened by the immediate application of a skin graft. Complete healing is obtained in a matter of days and the stage of infection and secondary contracture is eliminated.

When a segment of the mandible is to be removed the problem is twofold. Firstly there is the need to restore continuity of bone to conserve function, and secondly it is necessary to eliminate the cosmetic defect which such a resection can produce. Both of these desiderata can be met by the immediate insertion of a bone graft. The contraindications are either a grossly infected cavity or an opening in the oral mucous membrane communicating with the area of defect in the bone and incapable of accurate closure by suture.

The following cases were shown to illustrate these points:

Case I.—E. P., male, aged 53. A painless swelling had been present in 3–8| region for twenty-one months. Biopsy showed it to be an osteoclastoma.

12.2.52: *Operation.*—Resection of the alveolus posterior to 3| including the tuberosity, the outer wall and the bony floor of the antrum. A skin graft was immediately applied on a gutta-percha mould supported by a cap splint.

Discharged to outpatients in nine days. On the twenty-eighth day the splints were removed and the construction of a dental prosthesis commenced.

The minimal time spent in hospital, the freedom from discomfort and the early application of the final prosthesis are points worth noting.

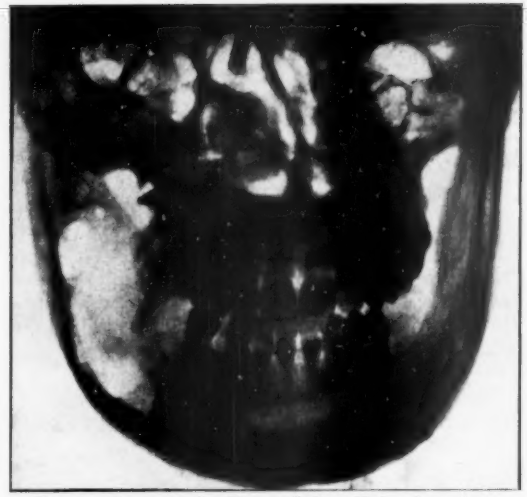

FIG. 1.—Pre-operative X-ray of *Case II* showing adamantinomatous involvement of the major part of the right ascending ramus and the body.

FIG. 2 (*Case II*).—X-ray appearances six months after resection and bone graft.

Case II.—M. O. S., female, aged 23. A swelling of the right side of the mandible had been noted for three months. There was an expansion of the mandible extending back from $\overline{4}$ to involve the whole palpable length of the bone. X-ray appearances were suggestive of a cyst (Fig. 1).

24.11.52: Intra-oral approach. The tumour was found to be mainly soft vascular tissue with some cystic areas. Through an external approach the jaw was resected from $\overline{3}$ at a point half an inch below the coronoid notch. The tumour had perforated the expanded bone on both aspects and it involved the mucous membrane. This area was resected. An adequate closure was not obtainable. The external wound was therefore closed and the left half of the jaw splinted to the maxilla.

Pathological report: Adamantinoma.

Seven weeks later the patient was readmitted. A bone graft was applied to restore continuity and contour. Discharged home thirty days later. After fifty days all splints were discarded.

X-ray appearances as shown (Fig. 2). Occlusion and appearance normal.

Case III.—E. H., male, aged 53. History of swelling and recurrent infection of the right ascending ramus for some years. Many previous intra-oral operations for drainage.

There was a large irregular swelling of the ascending ramus behind the angle involving both aspects with sinuses discharging pus into the mouth. X-ray showed marked multilocular cystic changes.

9.12.53: Resection of ascending ramus, condyle and coronoid from $\overline{8}$. This left a grossly infected cavity with fistulæ into the mouth. External wound closed. Anterior fragment of mandible splinted to the maxilla. Discharged to outpatients on the eighth day. Splints were removed on the fortieth day. Patient can obtain perfect occlusion. The jaw, however, deviates on opening, to the right. The occlusion is maintained only by the presence of the existing teeth, which are carious. It is felt that when these are lost derangement will occur. Bone graft, therefore, is to be carried out to restore position before the loss of these teeth complicates the method of fixation.

Mixed Salivary Tumours of the Palate.—STEWART H. HARRISON, F.R.C.S., L.D.S. R.C.S.Edin.

Introduction.—The mixed salivary tumour of the palate is often a malignant growth, locally invasive and frequently recurrent. Metastases are rare, but do occur.

Histology.—Of the five cases here reported, all showed cords and sheets of cells with little tendency to acinous formation, often embedded in a mucinous matrix and locally invasive.

Case reports: *Case I.*—Female, aged 39, with a history of deformity of left side of palate present for eight years. Rate of growth was slow until 1951 when tumour suddenly increased in size.

Operation (1951).—Half the palate was removed including the floor of the antrum which had been eroded by the tumour. There has been no recurrence and no metastases.

Case II.—Female, aged 64, with a history of swelling on the left side of the palate for an indefinite period which had recently increased in size. Fig. 1 shows half the palate involved in the tumour growth.

FIG. 1.—Mixed salivary tumour involving the palate.

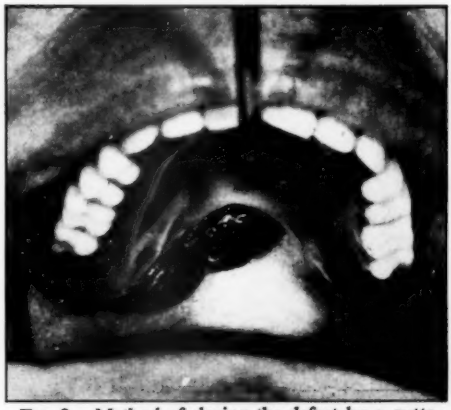

FIG. 2.—Method of closing the defect by a gutta-percha mould covered by a split skin graft attached to a denture.

Operation (1953).—Half the palate, including bone and alveolus, was removed. The defect was closed by a gutta-percha mould attached to a denture (Fig. 2) and covered by a split skin graft. Fixation was by a vertical steel rod passing from the denture to a plaster of Paris head-cape (Fig. 3). Fig. 4 shows the end-result. There has been no recurrence and no metastases.

FIG. 3.—Method of fixation.

FIG. 4.—End-result following excision of half the palate and lining of the defect with split skin graft.

Case III.—Female, aged 51, with a history of a swelling on the left side of the palate seen and removed in 1948. The tumour recurred in 1951 and again in 1954.

Operation (1954).—The left half of the palate including the underlying bone and the alveolus was removed. A small satellite tumour was found near the tuberosity. The defect was closed by a gutta-

percha mould covered by a split skin graft. An upper cap splint and a plaster of Paris head-cap were used for fixation. There were no metastases.

Case IV.—Male, aged 45, with a history of a tumour of the right side of the palate removed in 1945; this recurred in 1949.

Operation (1949).—Half the palate including the bony floor of the antrum which had been involved in the growth was removed. There has been no recurrence and no metastases.

Case V.—Female, aged 41, with a history of neuralgic pain for fourteen months, immediately preceding the apearance of a tumour on the right side of the palate.

Operation (1954).—Wide excision with a margin of healthy tissue. The bony floor of the antrum was found to have been eroded and this was removed. There has been no recurrence and no metastases.

SUMMARY

Sex. Age	Rate of growth	Recurrence	Duration of disease	Metastases
Female 39	Slow	Nil	8 years	Nil
Female 64	Slow	Nil	6 months	Nil
Female 51	Slow	After 3 years and after a further 3 years	6 years	Nil
Male 45	Slow	After 4 years	9 years	Nil
Female 41	Slow	Nil	Recent	Nil

CONCLUSION

In view of the high recurrence rate, the locally invasive character of these tumours and their resistance to radiotherapy, wide primary excision is advocated with a long follow-up period.

Grossly Comminuted Fracture of the Mandible: Two Cases.—GORDON L. FORDYCE, F.D.S. R.C.S.

Case I.—Civilian gunshot wound with comminuted fracture body of mandible.

Patient was transferred to the Plastic and Jaw Unit following an accident in which a 4.10 shotgun was discharged below his chin. An emergency tracheotomy had been performed prior to transfer and the patient was admitted within six hours of injury.

The soft tissue of the floor of the mouth and submandibular skin were grossly disrupted. The mental region was completely fragmented and $\overline{321}|\overline{1234}$ were missing. The body of the mandible was fractured horizontally in at least three planes bilaterally from the canine region nearly to the angle. The shot had penetrated the tongue, but had not progressed to the palate. The radiographic appearances on admission are shown in Fig. 1.

The patient was resuscitated and a general anæsthetic administered. The mandible was reconstituted by circumferential wiring around the fragments of the body of the mandible on each side. Interosseous wiring was employed to join the multiple fragments in the mental region to each other and to the main fragment and, in addition, these fragments were suspended to an arch wire, immobilized to the remaining mandibular teeth and the upper jaw. Intermaxillary eyelet wiring held the remaining teeth in normal occlusion. The soft tissues were approximated and the origins of the genioglossus and the geniohyoid muscles were identified and held forward by tying them over a button on the point of the chin (Mr. R. L. G. Dawson). Fig. 2 shows the post-operative X-ray. Six weeks later the intermaxillary fixation was removed and a lower cap splint cemented to the teeth to immobilize the mid-line fracture which had not united. The patient was discharged from hospital to attend as an out-patient.

At the fifth month union had still not occurred and a chip bone graft was inserted, giving established union in five weeks. Fixation was removed and a partial denture fitted.

Case II.—Gross comminuted fracture of the mandible with partial avulsion of the mental region.

History.—Four hours prior to admission patient was involved in a road accident. He was transferred in the prone position. Fig. 3 shows condition on admission.

Apart from the obvious injuries, the middle-third of the face was fractured along the fracture line of Le Fort I and Le Fort II. The right malar was depressed.

On the day of admission, under endotracheal anæsthesia, the mandible was reconstituted by direct interosseous wiring, interdental eyelet and intermaxillary wires. The malar was elevated by a temporal approach and the soft tissues of the tongue, floor of the mouth and of the face were repaired (Mr. J. E. Laing). A plaster head-cap and elastic chin-support assisted in immobilizing the middle-third of the face.

At five weeks the intermaxillary fixation was removed and a one-piece cap metal splint was cemented to the lower teeth to immobilize the fractures of the body of the mandible. This splint was left in situ and he was discharged from hospital.

At five months the lower splint was removed and the mandibular fracture was united (Fig. 4).

The operative treatment of these cases was carried out in co-operation with Mr. R. L. G. Dawson and Mr. J. E. Laing respectively, to whom I wish to make acknowledgment.

FIG. 1.—*Case I.*

FIG. 2.—*Case I.*

FIG. 3.—*Case II.*

FIG. 4.—*Case II.*

Mandibular Deformity Due to Skin Contracture.—IAN F. K. MUIR, M.B.E., F.R.C.S.

Patient aged 5 years. In spite of early skin grafting contracture of the front of the neck occurred following severe burns. The chin was pulled down on to the chest and the traction on the mandible had deformed the bone, causing an anterior open bite with fanning out of the lower incisor teeth.

Repair of the neck by a tubed pedicle flap was in progress. Photographs of two patients of similar age and with similar distribution of burns were shown, whose treatment had been completed. Anterior open bites had been present in both, but the condition had gradually corrected itself and when the permanent teeth had erupted the bite was normal. It was expected that spontaneous correction would also occur in the patient under consideration.

Three Cases and Models Illustrating a Technique for Precise Pre-operative Measurements in Mandibular Section for Prognathism.—B. W. FICKLING, F.R.C.S., F.D.S.

The advantages of resection of the body, over the more simple blind osteotomy of the ramus (Kostecka) were outlined. A small chip bone graft reduced the period of fixation by four weeks.

Pre-operative measurements.—Models of the patient's lower teeth are superimposed on a plaster model of a mandible. The height of the teeth from the lower border is checked with calipers on the patient, allowance being made for soft tissue cover. The upper teeth are articulated to this model mandible by means of a wax bite. The lower model is sectioned and the lower teeth placed in a new appropriate articulation, having especial regard to the effect on facial contour, both full-face and profile. The amount of bone to be removed from the mandible is represented by the gap resulting when the anterior fragment is replaced in its original occlusion (Fig. 1). Owing to deviation of the chin and the need to open or close the bite, these segments are commonly wedge-shaped.

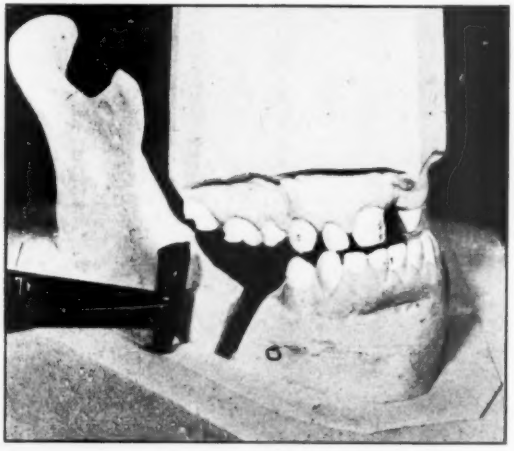

FIG. 1.—Models of patient's teeth mounted on a plaster mandible. The anterior fragment has been moved back to the new articulation, the sectioned fragments fitting in this position. On replacing the anterior fragment in the original occlusion, the section of bone to be removed is represented by the wedge-shaped piece of plaster, which exactly fills the gap.

Operation.—A submandibular approach is used. The mandibular nerve is exposed through a window and preserved. Metal templates of correct length are used to check the lines of the section, which is performed with dental fissure burs for greater accuracy. After fixation of the anterior fragment with dental cap splints the posterior fragments are immobilized with cap splints, dental wiring, extra-oral pinning or mandibular bone wiring according to the circumstances.

Bone graft.—In spite of meticulous accuracy and apposition of bone, fixation in earlier cases was required for nine to ten weeks. In the 3 cases shown a small bone graft from the iliac crest was employed in the form of bone chips laid around the line of section and over the window. In these cases the period of fixation was reduced to five to six weeks.

Case I.—R. A., aged 22. Prognathism. Section in $\overline{6}|6$ region, 7 mm. and 10 mm. Chip bone graft. Fixation five weeks. Firm union. Splints removed sixth week.

Case II.—M. M., aged 18. Apertognathia. 20 mm. Section $\overline{7}|7$ region. Chip bone graft. Fixation five and a half weeks. Firm union. Splints removed sixth week.

Case III.—H. H., aged 20. Prognathism. Section in $\overline{8}|8$ region, 13 mm. and 19 mm. Chip bone graft. Fixation six weeks. Firm union. Splints removed seventh week.

Section of Orthopædics

President—H. L-C. Wood, M.S., F.R.C.S.

[*March* 2, 1954]

Some Problems on the Borderline of Orthopædics

PRESIDENT'S ADDRESS

By H. L-C. Wood, M.S., F.R.C.S.

In a general hospital, the orthopædic surgeon comes in contact with many problems which are, strictly speaking, outside the realm of pure orthopædics or trauma. There is no subdivision of medicine or surgery with which we cannot claim some connexion either in diagnosis, treatment, or merely of a common interest in ætiology. It is with some of these borderline problems that this paper is concerned.

Maternal birth palsy.—This is defined as a partial or complete paralysis of certain groups of muscles in the lower limb, resulting from nerve injury during labour. Care must be taken to exclude other causes of paralysis such as pressure on the lateral popliteal nerve by a Clover's crutch, palsy after a spinal or caudal anæsthetic, or occasionally, hysteria.

Maternal birth palsy is an uncommon complication of parturition. In 1949 Chalmers collected 142 cases from the literature, an incidence of between 0·05% and 0·5% for all births. In four years, I have seen 6 patients with this complication, in a hospital handling 1,000 births per year. It is because for some time now our attention has been focused on disc protrusions as a cause of pain and paralysis that I wish to discuss this subject in some detail. The histories of these patients show a striking similarity.

In each case labour had been difficult and in all save one a forceps delivery had been attempted. This may appear to cast some reflection upon the type of midwifery being practised in my hospital, but these women were treated by different surgeons, all of considerable experience.

Only one woman had complained of sciatica during pregnancy and this had been mild and was on the left side. The muscle weakness, however, was invariably right-sided, and the symptoms were noticed within twenty-four hours of delivery. The time of onset was described in the notes as "on waking" or "noticed next day". After labour, sleep is natural, and, in addition, these patients had been anæsthetized, so that it is fair to assume that the paralysis was immediate.

The greatest muscle weakness was in the dorsiflexors. If it were due to root pressure, it follows that more than one root must be involved. Moreover the paralysis was maximum at onset and never increased, as might be expected from a disc protrusion.

Pain.—Pain during labour is not mentioned except in one instance, when cramp was experienced from buttock to knee. It was increased during uterine contractions and partially relieved by extending the leg against resistance. Pain in the leg did not persist for more than a few days.

In no case was backache a particular feature of pregnancy nor did it persist after labour.

The ankle and knee reflexes were only affected in the one patient who had the most severe paralysis. The ankle-jerk was absent, and the straight leg-raising test limited to 45 degrees on the affected side.

Sensory loss was variable, never severe, and usually transient. Signs in the back were conspicuous by their absence. Examination failed to show any scoliosis, limited movement, muscle spasm or the local tenderness commonly connected with disc protrusions, nor has late follow-up revealed any further symptoms in the back or legs.

In 1925 Lambrinudi read a paper on this subject to the British Orthopædic Association and later published it in the *British Journal of Surgery*. He quoted 2 cases, one of whom had been shown at a meeting of this Section by Mr. Laming Evans in 1923.

Lambrinudi thought that the symptoms were caused by stretching of the relatively fixed lumbo-sacral cord by backward rotation of the sacrum during labour. The ideas of veterinary surgeons supported this view. The cow is an animal in which paralysis of the hind-limb is sometimes noted after delivery and in which considerable rotation of the sacrum is said to take place.

It is, however, difficult on this theory to explain the fact that it is the right leg which is invariably affected. The fibres in the lumbo-sacral cord destined to supply the anterior tibial muscle are placed posteriorly, yet it is the anterior part of the cord which would be stretched most. Moreover, in the present small series, forceps delivery was carried out with the patient in the lithotomy position, in which the lumbar spine, hips and knees are acutely flexed—a position surely ideal for relaxation rather than stretching of the lumbo-sacral cord.

O'Connell in 1944 suggested that some cases, at least, could be explained by lumbar disc protrusions, occurring during labour. He quoted 4 women, all of whom had had attacks of lumbago and sciatica before pregnancy, and in whom severe symptoms did not arise until a week or more after

labour. The disc protrusions were confirmed at operation. These cases are those of sciatica complicated by labour, and are not a complication of labour. They do not fall into the same category as those under discussion.

The late onset of symptoms has been used as an argument against direct pressure by the fœtal head or the forceps blade, upon the lumbo-sacral cord. In the present series the onset was never later than the following day.

There is other evidence in support of direct pressure.

When the abdomen is opened it is easy to feel the lumbo-sacral cord as it crosses the pelvic brim in the triangle of Marcille. X-ray studies during forceps delivery have shown that the tip of the forceps blade can approach to within 9 mm. of the sacral promontory and could easily come in contact with the nerve. However, it is certain that this complication can happen during a non-instrumental delivery.

The relative prominence or flatness of the sacral promontory can be shown by routine pelvimetry. It is the promontory which guards the nerve from pressure of the fœtal head but not necessarily from the forceps blade. When the promontory is flat, damage is more likely. I am told that in midwifery it is usual to apply the left blade of the forceps first, guided by the hand of the operator. The blade entering the right side of the pelvis is applied with greater difficulty. This fact may account for the frequency of right-sided lesions.

Although there may be several explanations for maternal birth palsy and sciatica I feel certain that these are six examples of a condition which constitutes a complication of obstetrical management.

Backache.—The orthopædic surgeon may be asked for an opinion upon a woman who is pregnant and who gives a previous history of lumbago or of sciatica. There may be a clean-cut story of a previous disc protrusion. The questions we have to answer are usually two: Should the pregnancy be terminated? Should a Cæsarean section be performed?

I have been asked, on more than one occasion, whether pregnancy should be terminated in a patient who has had previously a severe sciatica diagnosed as due to a disc protrusion. I cannot believe that termination of pregnancy is ever justifiable on this ground. My experience has been that these women have gone through a normal labour without trouble and have not experienced a repetition of their sciatica after delivery.

Should a Cæsarean section be performed? Here again, the history of previous disc trouble is not an indication. I have not seen any woman who had acute sciatica which could be attributed to labour and which might have been prevented by a Cæsarean operation. Those women who suffer from sciatica during the late months of pregnancy, have, of necessity, to rest, sometimes in bed, during the last few weeks. If afterwards the sciatica persists, removal of a disc protrusion may be advisable, but it is usually found that after a normal delivery the sciatica is cured. In any event, why have two operations, when one will suffice?

The relation of backache to gynæcology is much more nebulous. If we teach that in the absence of gross gynæcological disorders, a patient who has backache has something wrong with her back we shall not go far wrong. The simple rectal examination, which we should all do, in anyone with low back pain, should be sufficient to eliminate the more gross of these disorders. We can at least feel a large pelvic mass, but would probably not detect minor degrees of uterine retroversion, or prolapse—nor does this matter, because I do not believe that severe or persistent backache is caused by such displacements. We all see patients who have had corrective operations or even hysterectomy but whose backache remains. The onus of cure is on us.

Let us therefore remember that when it is a case of "doing something" a well-fitted corset is cheaper, warmer and more effective than short-wave diathermy, and moreover can be used to suspend the stockings.

Remaining in the pelvis a little longer I now turn to some

Orthopædic complications of urology.—During the last few years some 14 cases of bone and joint infection following urological surgery have come to my notice.

A.	Osteitis pubis		9
B.	Osteomyelitis of vertebra		2 + 1 after pneumonia
C.	Infective arthritis:	Shoulder	1
		Hips	2

Osteitis pubis is a complication of pelvic cellulitis first described in the English language by Beer in 1924 and in France by Legan and Rochet in 1923. The condition is found in both sexes, and is not always an operative complication. The most usual type, however, is that following prostatectomy, and the incidence of this type appears to have increased in recent years, since the introduction of the retropubic operation. In 1950 Millin reported an incidence of 0·82%, but other authors have reported an incidence as high as 16%. The entity has been described as an orthopædic disease sponsored by urological surgeons.

The onset is usually between four to eight weeks after the operation, and the patient has, therefore, probably left hospital. Because of this delay, the symptoms may not be associated with the previous disease or its treatment.

Severe pain is felt in the region of the symphysis pubis and groins, and radiates down the obturator nerves. Adductor spasm is a common feature and the patient may complain of inability to abduct the thighs. Walking becomes difficult or impossible. At a later stage the tubera ischii are involved, with spasm of the muscles of the pelvic floor. There is pain on micturition or defæcation, and radiation down the back of the thighs. Sitting down is agony. A diagnosis of sciatica or obturator neuritis may be made.

On examination there is marked tenderness over the symphysis pubis and ischial tuberosities. Hip movements may be limited. This is most often due to obturator spasm, although spread of the disease to the hip-joints has been described. In 2 cases reported by Millin the vertebræ were also affected. The suprapubic wound is often soundly healed, but there may be a history of previous infection. There is always pyrexia, and the E.S.R. is raised to a high level. X-rays may be of little help at first, but after the third week the characteristic osteoporosis and widening of the symphysis is evident. At a later stage there is a deposition of irregular periosteal new bone from the symphysis to the tuber ischii. Sequestra formation is rare, but in one case in this series, a sequestrum was clearly visible (Fig. 1).

With such history and physical signs, the diagnosis can be little in doubt, but one or two points in differential diagnosis should be mentioned.

FIG. 1.—Osteitis pubis. Widening of symphysis.

FIG. 2.—Tuberculous disease. Sinus filled with Lipiodol.

Tuberculous disease (Fig. 2) in this area may be associated with a sinus, whereas a sinus after prostatectomy will be closed before the onset of osteitis. Moreover the tuberculous sinus is unlikely to be suprapubic in position. Tuberculous disease tends to be unilateral, in contrast to the bilateral changes seen in osteitis pubis.

Frank osteomyelitis of the pubis may occur and is likely to be accompanied by abscess and sequestra formation.

By far the most important point in differential diagnosis, however, is to remember the likelihood of secondary deposits from the prostate. These are not always of the typical sclerosing type and may cause symptoms before their presence can be confirmed radiologically. When suspected, a trial of therapy by stilbœstrol in large doses of at least 100 mg. per day should always be made. This may have the twofold advantage of curing the pain, and at the same time making the radiological appearances more obvious.

Many and various theories have been put forward to explain the manifestations of osteitis pubis. Mortensen (1951) mentions retropubic hæmorrhage, extravasation of urine or abscess formation, preceding the onset of osteitis. In the present series one case followed a forceps delivery in a young woman, another followed pneumonia in a middle-aged man.

Local trauma, by retractors, tearing of the rectus abdominis, or rupture of the pubo-prostatic ligament has been suggested as a cause. In support of this theory of trauma, Adams and Chandler (1953) have described a case of traumatic origin in an 18-year-old male. The trauma was that of running on an indoor race track at High School, one year previously. The appendix was removed but failed to relieve pain, which recurred upon further exertion. Walking and running caused pain and the gait became waddling when fatigued. X-ray at this time showed a destructive lesion in the pubic symphysis and the interpretation of a biopsy indicated a diagnosis of chondrosarcoma. The area was excised, but further histological study showed merely low-grade inflammatory reaction,

with bone absorption and fibrosis. (This is in accord with one case in my series who died from pulmonary embolism. At autopsy the bone was soft and fibrotic and organisms were cultured from it.)

Four other cases due to trauma were found in the literature in male or female patients all under 30, but in each case the trauma was of slight degree. In one of these cases the osteitis proceeded to abscess formation.

It is suggested that local vascular thrombosis predisposes to infection of the bone, which is poorly supplied with blood in any event.

In the present series of 9 patients, 5 of the 7 post-operative cases had heavily infected urine, or wound infection, or both, the infecting organisms being of the *B. coli*, proteus or pyocyaneus group.

It would seem, therefore, that this condition is of infective origin and that trauma is an important contributory factor.

Treatment.—Pain is relieved by rest. The appropriate antibiotic is worth a trial. Reopening and drainage of the retropubic space appears to give dramatic relief even if pus or obvious infection is not found. The progress to complete cure is slow, and may take a year or more.

I have 5 cases in which genito-urinary surgery has been followed by sepsis in sites other than the pelvis. One in the shoulder—who unfortunately cannot be traced. Two in the hip, and two in the vertebræ.

A man of 64, following the operation of partial cystectomy, developed a pelvic abscess which discharged *per rectum*. During convalescence, he felt pain in the right hip. No immediate treatment was given but after a steady increase of symptoms over several months the pain became so severe that the hip was immobilized in a plaster spica. There was pyrexia up to 100° F., and the E.S.R. was 75 mm. in one hour (Westergren). Five weeks later the temperature had settled and the E.S.R. was 22. X-ray showed a narrowed joint space. Some months later an arthrodesis by the two-stage method of Watson-Jones was undertaken. Section of the much thickened capsule showed it to be avascular, with no recent inflammatory change. Recovery from the operation was uneventful and a firm ankylosis seemed assured.

Some months later while mowing his lawn, pain was felt, followed by an abscess over the right great trochanter (Fig. 3). The nail was removed and when the track had healed a painless joint was obtained with about 30 degrees of free flexion. The organism grown from the pus was *Staph. aureus*. The patient now leads an active life and apart from two small superficial "flares" is quite comfortable.

FIG. 3.—Right hip. Infective arthritis following pelvic sepsis.

FIG. 4.—Osteomyelitis of vertebræ following pneumonia.

The second case of hip-joint involvement was that of a man in the middle fifties who elected to have his prostatectomy done by the local practitioner in a small hospital abroad. Because of brisk post-operative hæmorrhage the bladder was "packed". Unfortunately the packing was forgotten and was later seen through a cystoscope. Removal was effected by grasping with forceps and dragging it out through the urethra. This surgical manœuvre was followed by pelvic cellulitis and so much constitutional disturbance that pain in the hip-joint, at the time, was almost unnoticed. Continued pain and increasing stiffness caused an X-ray to be taken, and it was then discovered that a non-suppurative, destructive arthritis was in progress. No treatment, apart from bed rest, was given and the patient is now walking painlessly with the aid of a stick. The range of free flexion is 40 degrees.

The vertebral cases have similar histories. Both elderly men, the one following stricture dilatation, the other retropubic prostatectomy.

There was an insidious onset of pain in the back within a few weeks of operation, which gradually increased in severity but responded to rest in a plaster shell. In the early stages no radiological changes

were seen, but later a destructive lesion became evident, which progressed to complete bony fusion with osteophyte formation. One of these patients died a few months afterwards from a stroke, the other has been traced and is symptom-free six years later.

A further case of vertebral osteomyelitis was that of a man of 60, who, following pneumonia, developed pain and dorsal kyphosis four months later. When first seen he had a high swinging temperature and an E.S.R. of 115 mm. (Westergren).

Radiography showed vertebral collapse (Fig. 4) and a shadow suggested a paravertebral abscess. Costotransversectomy revealed a mass of granulation tissue but no pus. Treatment by rest, together with penicillin, relieved symptoms, and within eight months solid bony fusion was obtained. Recent examination showed the patient to be cured.

There are few recorded cases of this type. Wear *et al.* (1952) have reported 33 patients suffering from pyogenic osteomyelitis of the spine, without particular reference to the site of the original infection. In 1950 Hurwitz and Albertson reported a case of cervical osteomyelitis with urinary tract infection, and quoted 6 others. The patients in my series illustrate the prominent features of this type of osteomyelitis namely:

An unrecognized acute stage, undiagnosed symptoms of considerable duration, often not related to the spine. Pain might be referred to the chest, abdomen or the hip. Gross suppuration is conspicuously absent, and the prognosis in this type of metastatic osteomyelitis is comparatively favourable. In the spine the characteristic radiographic appearance is of concomitant bone destruction and osteoblastic response, so unlike early tuberculous infection. Total destruction of the intervertebral disc is usual, but vertebral collapse sufficient to produce clinical deformity is, however, rare. While in tuberculous disease, paravertebral abscess and spread beneath ligaments are common, this is not so in pyogenic infections. Moreover, erosion of the anterior surface of the vertebra is not seen. Psoas abscess is said to occur but I have not seen one.

Mode of spread.—The direct route between the pelvic organs on the one hand, and the hip-joints and vertebræ on the other, is thought to be by the venous system. Batson (1940), by injection of the dorsal vein of the penis in human cadavers and in living monkeys, demonstrated the existence of a continuous system of veins linking the pelvic venous plexus with that of the vertebræ. He called this the vertebral venous system (Fig. 5), thus making four venous systems: caval, portal, pulmonary and vertebral, the latter extending from the pelvis to the skull. Metastatic spread from the pelvis is thus explained.

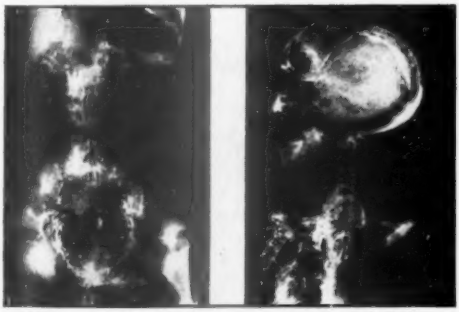

FIG. 5.—Vertebral venous system. Injected specimen (Batson).

There are other links between diseases of the urogenital tract and skeleton. Tuberculosis is an obvious example.

Recent work by Romanus of Stockholm (1953) upon the relationship between ankylosing spondylitis and genito-urinary infection is worthy of note. This author has reviewed 117 patients in an exhaustive monograph. He has coined a new term—Pelvo-spondylitis ossificans—which he differentiates sharply from rheumatoid arthritis and believes to follow a primary septic focus in the prostate and seminal vesicles, not necessarily gonococcal in origin. He considers that the spread to sacro-iliac joints and spine can best be explained by the vertebral venous system rather than by the lymphatic route, and that the peripheral symptoms of pelvo-spondylitis manifest in joints, tendons, subcutaneous tissue, and the eye are caused by toxic spread in the general circulation.

These latter symptoms bear a striking resemblance to those found in acute gonorrhœa or in Reiter's syndrome. His theory is at some variance with that commonly held—namely that the changes in these structures are a general allergic response. The stimulus is unknown and is not necessarily of infective origin. The affection of joints, tendons and mucous surfaces has been grouped together by some authors under the heading of the mucocutaneous syndrome, but a similar response can occur in connective tissue.

Two unusual malignant deposits in bone have come to my notice. The first appeared as a swelling of the lower end of fibula (Fig. 6), in a man of 63 who gave a history of hæmaturia for three years. A bladder tumour had been diagnosed both by cystoscopy and biopsy as a benign papilloma. Examination of the bone tumour proved it to be a well-differentiated transitional cell carcinoma with squamous metaplasia. In this case we were able to foretell the true nature of the bladder growth by several months.

A second squamous cell carcinoma of bone, not of genito-urinary origin, occurred in a patient who had had a resection for carcinoma of the œsophagus eighteen months before. The complaint

was of severe pain in the hip. An X-ray revealed a cystic condition of the femoral head thought to be malignant (Fig. 7).

FIG. 6.—Deposit of squamous cell carcinoma from bladder.

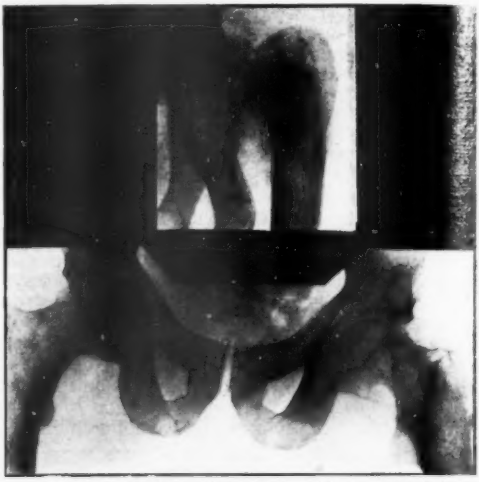

FIG. 7.—Early and late views of destructive lesion in hip. (Carcinoma of oesophagus.)

Biopsy showed that the histology of the affected bone was identical with that of the primary œsophageal growth.

This patient died, not of œsophageal stricture and starvation, nor of other secondary deposits, for at autopsy there was none—but of morphine poisoning. Reflection shows that had a bold attack been made upon this hip, and an excision of the femoral head and neck been undertaken, the patient might be alive to-day and would, at least, have been spared much pain.

On more than one occasion radical surgery performed on what appeared to be a solitary metastasis has been well worth while.

Combination of joint and skin disease.—The occurrence of arthritis in the small joints of the hand or foot together with psoriasis is more common than the surgeon would believe, as it is usually seen by the dermatologist.

Skin lesions should always be looked for when faced with multiple joint swellings. Some long-standing cases of psoriasis may show disorganization of the joints with bone atrophy sufficient to allow telescopic movement. This is the classical main en lorgnette of Marie and Leri. More recently the same condition has been described under the name of Arthritis Mutilans (Nielsen and Snorasson).

It is of convenience to group in one's mind some similar diseases associated with bone atrophy or destruction of small joints:

(1) *Trophic bone atrophy in*:
A. Syringomyelia. B. Tabes. C. Diabetes. D. Leprosy. E. Psoriasis
(Tendency to involve terminal phalanx and sometimes interphalangeal joints).
(2) *Arthritis mutilans* with polyarthritis, without evidence of nerve or skin lesions.
(3) *Vascular disease* of the Raynaud type with scleroderma.

Skin lesions are found in many diseases of the skeleton, the café-au-lait patches of Albright's disease, pigmentation in neurofibromatosis and in scleroderma, to mention a few.

Reiter's syndrome of non-specific urethritis, eye and joint changes, sometimes associated with skin lesions—keratodermia blennorrhagica—has been variously attributed to venereal disease, Flexner dysentery and other infections. It is probable, however, that the urethritis is but a manifestation of some general response to a variety of ætiological factors, and not due to local infection.

The connexion between *bone and joint disease and the eye* is well known.

With the generous co-operation of my ophthalmic colleague, Mr. L. H. Savin, I am able to show these tables and illustrative drawings, which are self-explanatory.

DISEASES OF BONES AND JOINTS WITH EYE CHANGES

A. *The eye disease spreads to the joints.*—(1) Gonococcal Ophthalmia. (2) Pneumococcal Conjunctivitis.

B. *Common origin of infection.*—(1) Food—Brucellosis, Dysentery, Typhoid (Conjunctivitis, Iridocyclitis). (2) Tuberculosis—Phlyctenular Conjunctivitis.

A. *The eye disease spreads to the joint.*—Fig. 8 illustrates at a glance, the spread of ophthalmia neonatorum or of pneumococcal conjunctivitis, to the joints of the limbs, more often on the left than on the right side.

FIG. 8.

B. *The common origin of eye and joint changes* is illustrated by those occurring in food poisoning, or in tuberculosis. In the latter almost any part of the eye may be affected, though not visibly so. The presence of phlyctenular conjunctivitis suggests that there is latent tuberculous infection elsewhere, and should put us on our guard. It is a rare phenomenon, and not usually mentioned in orthopædic textbooks.

C. *Infectious and contact diseases*—Iritis, conjunctivitis, keratitis.—(1) Gonorrhœa—arthritis second and third week, while urethritis active. (2) Measles—joints, conjunctivitis, corneal ulcers. (3) Syphilis. (4) Leprosy—joints, iridocyclitis.

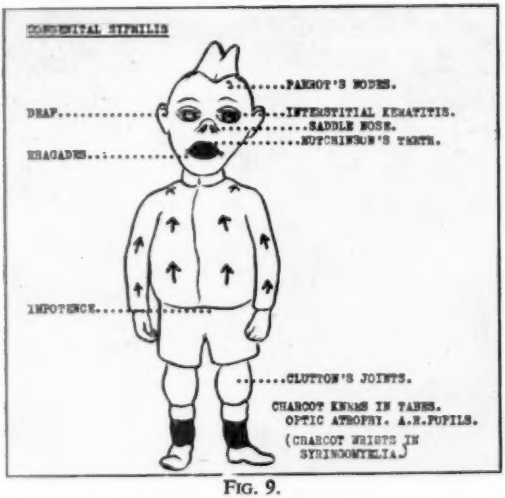

FIG. 9.

It is perhaps worth remembering that the diagnosis of an acute gonococcal joint should not be made except in the presence of active urethritis. In chronic joint swellings, the complement-fixation test is, in my experience, almost invariably negative.

Syphilis.—The gentleman from Dartmoor speaks for himself and only wants a gumma to complete the picture! (Fig. 9).

Unknown ætiology.

(1) *Rheumatoid arthritis* (Fig. 10).—The occurrence of iridocyclitis with rheumatoid arthritis and

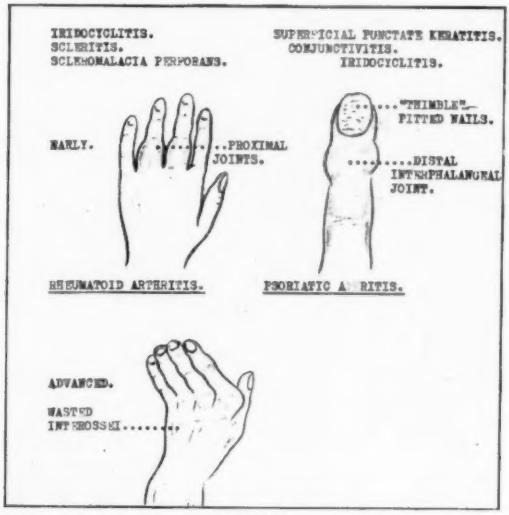

FIG. 10.

with Still's disease is less common than in ankylosing spondylitis, being about 4·7%. Still, in his original paper, did not mention eye changes. In ankylosing spondylitis the incidence varies according to the time which the disease has been present. Thus in young men it is not common; but over the age of 45 years, more than 50% of spondylitic patients have also had iritis. In the early stages this responds well to local cortisone therapy but it can be a great disappointment, when after perhaps many operations, on joints or spine, our efforts are foiled by blindness.

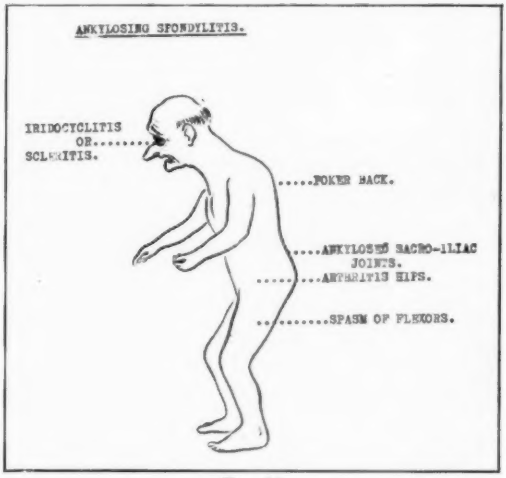

FIG. 11.

The vision in some spondylitics (Fig. 11) with gross kyphosis is faulty, partly owing to the posture, but also due to opacities in the anterior chamber of the eye, which are floating near the centre of the

cornea. If the kyphosis is corrected by an osteotomy and the posture improved, these opacities will fall to the lower part of the cornea and thus the vision will be much improved: another reason for doing an osteotomy of the spine.

(2) *Sjögren's syndrome.*—Dryness of the eyes is sometimes observed in elderly patients with rheumatoid arthritis, and this may form part of the disease described by Sjögren—*kerato-conjunctivitis sicca.* In the complete syndrome the mucosa of the mouth, nose and larynx is also dry and the salivary glands are enlarged. The relationship to rheumatoid arthritis is doubtful, but Kellgren states that probably about 10% of elderly patients have mild symptoms. Treatment with cortisone has not produced dramatic improvement in the eyes, but one patient was enabled to spit after twelve years of abstinence.

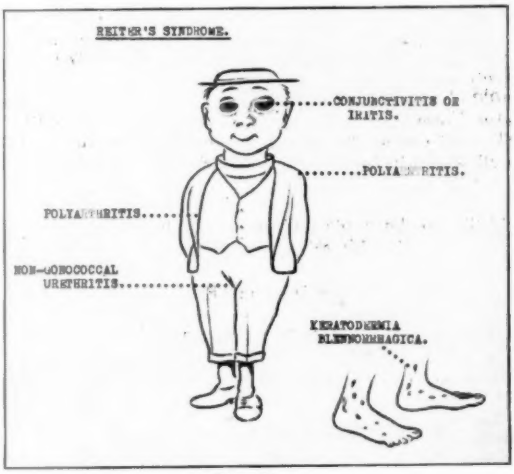

FIG. 12.

(3) *Reiter's syndrome.*—This has already been mentioned in connexion with keratodermia blennorrhagica. Fig. 12 is merely to remind us to look for conjunctivitis in connexion with polyarthritis, and to emphasize that the disease is non-gonococcal, but may be venereal, in spite of the gentleman's collar and hat. However, the urethritis can be regarded as one manifestation of a general

FIG. 13.

response to some morbid process involving mucous surfaces of urethra, eyes and joints—one example of the so-called mucocutaneous syndrome.

(4) *Gout* (Fig. 13).—We remember the hot joints of gout but not perhaps the hot eye. It is suggested that both are allergic manifestations, common in families possessing an anomaly of purine metabolism.

ALLERGIC GROUP

Allergic.

Erythema multiforme—joints—conjunctivitis—skin lesions
Purpuras—Schönlein
{ Palindromic rheumatism
{ Intermittent hydrarthrosis—œdema of lids—iritis, may precede rheumatoid arthritis

In this last and rather vague group, I shall merely draw attention to the fact that intermittent hydrarthrosis may be a precursor of rheumatoid arthritis, as also may be the œdema of the eyelids, or iritis which may accompany it.

I have recently been told of another example of allergy in a personal communication from Dr. J. A. Keeping of the Paddington Chest Clinic. She has had seven patients who presented with tenosynovitis about the wrist or ankle. This soon cleared up but shortly after three of these patients developed active pulmonary tuberculosis, while in the others, the Mantoux reaction converted to positive within a few months.

In conclusion I would like to thank my colleagues at King's College Hospital and elsewhere for their help in the preparation of this address.

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Bone and Joint Changes in Psoriasis

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Editorial of the British Medical Journal, dated 11th April, 1953, page 823.

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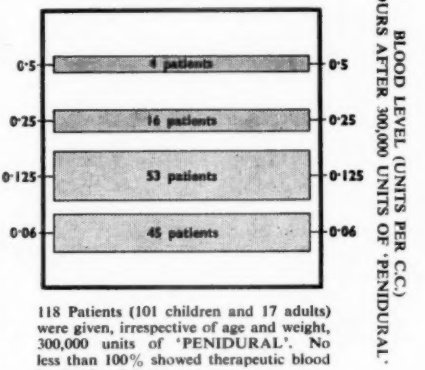

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Section of Otology

President—R. R. SIMPSON, F.R.C.S.Ed.

[*March 5*, 1954]

DISCUSSION: CONGENITAL DEAFNESS [*Abstract*][1]

Professor A. A. J. van Egmond:

After discussing the meaning of the expression congenital deafness, the speaker defined the condition as a more or less marked loss of hearing, present at birth, hereditarily transmitted or caused by environmental influences during the prenatal period and leading to mutism. The hereditary and environmental factors are interacting and often it is difficult to separate them.

Hereditary congenital deafness may be considered in two groups:

A. *Dominant inner-ear deafness.*—This develops nearly always at middle age. It is "congenital" only as being one of the six characteristics of the hereditary syndrome, first described in 1951 by Waardenburg.

According to Mendelian laws, due to its dominance inner-ear deafness will be present in every generation with a 50% chance for the offspring to acquire it also.

B. *Sporadic recessive deafness* is so called because often only one child in a seemingly healthy family is affected, without the cause being known. The speaker demonstrated how such a sporadic case of deafness may arise and how it may be influenced by consanguinity.

No standard picture of these two types of deafness can be given because both groups show many differences and transitions between the anatomical factors.

In dominant hereditary deafness the development of the cochlear bone is arrested with subsequent defects of the cochlear nervous tissue and malformations of the membranous connective tissue, whereas the acoustic nervous system is intact. In recessive sporadic deafness, on the other hand, the total acoustic nervous system, i.e. the nerve fibres, the nerve trunks, the central nuclei and tracts are affected, whereas the cochlear bone is intact. In both groups the organ of Corti is more or less damaged which explains the variable degree of hearing loss.

Congenital atresia auris causes congenital deafness if it is bilateral. In some cases this anomaly seems to be dominantly hereditary. In most cases, however, the affection is probably acquired *in utero*. The anatomical abnormalities are principally situated in the middle ear. Consequently a conductive deafness arises, that may be improved by fenestration.

Erythroblastosis fœtalis may also constitute a cause of congenital deafness. In this affection the child may show, a few days after birth, an icterus gravis and signs of central nervous system damage, eventually resulting in a neurological symptom complex, called kernicterus. These lesions may also be situated in the nuclei of the cochlear pathways, resulting in a more or less severe impairment of perceptive deafness.

Environmental factors come into play especially in the first 8–12 weeks of pregnancy. In this period all the organs and systems acquire their definite shape; the still undifferentiated cells are highly vulnerable. At this period, virus infections may cause congenital cataract and congenital deafness.

Syphilis may also constitute a cause of congenital deafness, although the onset of deafness is generally later, at the age of 8–12 years. *Endemic cretinism*, formerly considered as a cause of a dominant hereditary deafness, has appeared to be caused principally by prenatal iodine deficiency.

The diagnosis of congenital deafness is mainly based on the anamnestic data obtained from the parents, as its diagnosis by objective signs has hitherto failed. It may be prevented by improving the social and hygienic conditions during pregnancy, so that infectious diseases may be avoided. Active immunization, before marriage, against rubella and other infectious diseases, passive immunization during pregnancy in epidemic periods, the induction of abortion, when the disease is actually contracted during pregnancy, these are all possibilities for consideration.

It is impossible to cure hereditary congenital deafness. The frequency can only be reduced by social measures, the most drastic of these eugenic measures being sterilization. Consanguineous marriages must be avoided.

Mrs. Florence Cavanagh:

The Rhesus Factor and Deafness

The Rhesus factor is an antigen on the surface of the erythrocytes of 85% of the white population. These 85% are Rhesus-positive individuals. The 15% without the Rhesus factor are Rhesus-negative.

[1] See *J. Laryng.* (1954) **68**, 429, 444, 461.

Note.

When a Rh−ve woman marries a Rh+ve husband, she is likely to have Rh+ve children. During such a pregnancy some Rh+ve fœtal erythrocytes pass through the placental barrier into the maternal blood and there provoke the production of antibodies. These antibodies then pass back into the fœtal blood. The antibody titre rises as the pregnancy progresses, but may not reach a dangerous level until later pregnancies.

When the Rhesus baby is born he is manufacturing his own Rh+ve erythrocytes, but his serum also contains antibodies from his mother. These antibodies combine with his red cells and cause haemolysis. This has two obvious effects—first he becomes anæmic; secondly, the pigment freed by haemolysis causes jaundice. An affected Rhesus baby often appears normal at birth and yet within a few hours becomes deeply jaundiced, goes limp and drowsy, has cyanotic attacks, begins to twitch and has convulsions, develops a high-pitched "cerebral" cry and shows signs of spasticity in the limbs—all the clinical signs of kernicterus. In the past, many such cases died, but those surviving were often spastic, athetoid or mentally retarded. Only recently has deafness been noted amongst these patients.

Post-mortems on babies dying of severe neo-natal jaundice show yellow pigmentations of parts of the brain. Children who recover from this condition of icterus gravis and die years later, have no such pigmentation, but in the corresponding regions one finds degeneration and necrosis of cells with subsequent shrinkage of the areas. The auditory pathway is widely involved, often symmetrically. The dorsal and ventral cochlear nuclei show cell injury, also the medial geniculate bodies. The trapezoid body and lateral fillets show reduction of fibres.

The treatment of the affected Rhesus baby is obviously urgent, if serious and permanent damage to the brain is to be prevented. Nowadays, these babies are given an exchange transfusion—using the umbilical vein—about three hours after birth. Some 300 c.c. of Rh−ve blood is used. (If Rh+ve blood were used, this would combine with the circulating antibodies and cause further hæmolysis.)

In this investigation three groups of children were studied. Group I consisted of Rhesus babies born at St. Mary's Hospital, Manchester—the main Maternity Teaching Hospital of the Region, which is close to the Blood Transfusion Centre, and where the babies are in the care of the Professor of Child Health. These children, therefore, had the most up-to-date treatment, given at the earliest period. 82 such children were examined for deafness.

The second group, examined at the Duchess of York Hospital for Babies, consisted of children whose Rhesus sensitization was not diagnosed until after birth, days and even weeks later. These Rhesus babies have suffered more extensive damage, and a higher incidence of deafness might be expected. There were 42 children in this group.

The third group consisted of known deaf children. Each mother was asked for details of the first two weeks of the baby's life, and samples of blood from mother and child were sent to the Regional Transfusion Centre to determine whether there was evidence of Rhesus incompatibility. 118 deaf children were seen.

In Group I the 82 children were between 1 and 5 years of age. 13 had speech defects suggestive of high tone deafness, and were referred to Professor Ewing. 2 had a hearing loss of less than 20 decibels; 1 a loss of 25–30 db; 1 a loss of 40–50 db on the left, 20–30 db on the right. One child, grossly retarded mentally and physically, may well be deaf, but was impossible to test. At the most, there are only two deaf children amongst 82, about 2·5%.

In Group II we have the unfortunate babies who received treatment late or not at all. 30 of these were examined with their siblings. Amongst the siblings, 12 unsuspected cases of Rhesus sensitization were found, i.e. 42 affected patients. 11 children had suggestive speech defects, and 4 are deaf. 1 has the typical audiometric chart of the literature with a steep drop for the high frequencies; 1 a uniform loss of 45–50 db; 1 a loss up to 50 db for the high tones on one side only; 1 a slight to moderate loss. This is an incidence of nearly 10%—considerably higher than in the better treated group.

In Group III 118 severely deafened children were seen, and the cause of deafness in 51 seemed fairly clear (meningitis, mumps, rubella of pregnancy, &c.). Of the 67 remaining, 11 children had histories suggestive of Rhesus sensitization—jaundice, drowsiness or reluctance to feed. None had any of the dramatic symptoms. Amongst these 11, the combination of Rh−ve mother with a Rh+ve child was found in 4 cases, but in one the mother had no antibodies. There are, therefore, 3 cases of deafness probably due to Rhesus incompatibility amongst 118 deaf children—not a high incidence perhaps, but in fact equal to that of maternal rubella in this series.

Professor John R. Lindsay and Mr. M. Spencer Harrison:

The Pathology of Rubella Deafness

Carruthers (1945) was the first to describe definite pathological changes in the temporal bones in rubella deafness in children and Nager (1952) followed with two cases showing similar pathology. It is interesting that one of these latter cases appears to show interference with development at a considerably earlier stage than the other. Lindsay *et al.* (1953) found that only 1 out of their 5 cases showed any notable pathology in the temporal bones.

Histopathology

The bony labyrinthine capsule is always normal. No abnormality has been demonstrated in the utricle or semicircular canals. Reissner's membrane is often collapsed and may be adherent to Corti's organ.

The stria vascularis varies considerably in the different coils, in some it is almost absent, in others less than half of its normal area may be present.

Corti's organ is also variable in appearance though the general contour is usually well preserved. The greatest defects appear to be in the apical coils which are later in the scale of development than the basal portion. The cells of Deiters, Hensen, and Claudius are fairly normal. The pillar cells are incompletely developed in the apical coils. Post-mortem degeneration renders clear definition of the hair cells difficult but it is likely they are particularly affected by the lack of development in the apical regions.

Changes in the tectorial membrane are very evident; frequently it is rolled up against the limbus over the teeth of Huschke in contact with the collapsed Reissner's membrane and encased in a sheath of flattened cells similar to those normally covering the limbus. The membrane may, however, be tucked into the internal spiral sulcus and though it does not often reach the organ of Corti it may be attached across the scala media to the stria vascularis.

The cells of the spiral ganglion and the nerve fibres do not appear to be affected by the process.

The changes in the saccule are often marked. The lateral wall including the reinforced area of Perlman may be hypertrophic and may show irregular adhesions to the macula which is itself degenerate in these areas. At times the saccule is collapsed, but the lumen may be unchanged.

Discussion

Rubella in the first trimester of pregnancy thus produces in the child changes similar to the Scheibe or sacculo-cochlear type of malformation of the inner ear. This closely resembles an hereditary type of malformation seen in certain varieties of dog. In these the changes found within the cochlear duct appear to be secondary to changes in the stria vascularis with a resulting collapse of the cochlear duct and saccule, indicating a lack or even absence of endolymph. In the dog the tectorial membrane and Corti's organ are abnormal throughout—evidence of development arrested in an earlier stage than in the rubella lesions. In other ways the two conditions are probably identical.

The limitation of the stria vascularis occurring in the rubella lesion is likely to be compatible still with the maintenance of normal endolymph and normal function of structures within the cochlear duct. Crowe, Guild and Polvogt (1934) state that a considerable degree of atrophy of the stria vascularis must be present before any effect on the hearing can be demonstrated. Also extensive atrophy of the stria vascularis was present in Day and Lindsay's (1949) case of Ménière's disease which had good hearing. However the marked limitation of the extent of the stria may be interpreted as an indication of the action of the rubella virus.

Interference with function may be accounted for by the incomplete development of Corti's organ in some areas and by the pathological state of the tectorial membrane. Even in the areas in which the organ of Corti appears normal it is unlikely that, with an abnormal tectorial membrane, its functions could be maintained.

In spite of lack of development of the pillar and hair cells in both rubella deafness and hereditary deafness in dogs no abnormality has been shown to occur in the peripheral cochlear neurone. In traumatic deafness in cats degeneration of the pillars is rapidly followed by degeneration of the neurone (Schuknecht *et al.*, 1951; Schuknecht and Sutton, 1953).

Tectorial membrane changes similar to those shown are seen in experimentally deafened cats and in children deafened in early life by conditions such as virus diseases. It has already been noted that the same change can occur in hereditary deafness in dogs and is thus associated with several forms of deafness, but is not the only lesion found in the cochlea in any one of the conditions already mentioned.

There appears to be no evidence indicating that the cochlear lesions described can be attributed to post-hydropic degeneration as postulated by Wittmaak or that hydrops ever occurs in these ears. In certain experimental injuries to the ears of monkeys and rabbits it has been shown that relatively mild degrees of inflammatory reaction in the perilymphatic fluids may produce extensive degeneration of both the primary cochlear neurone and the structures in the cochlear duct with no significant degree of hydrops. In contrast an extensive hydrops is seen in Ménière's disease without any histological evidence of degeneration of the primary cochlear neurone.

It would appear from the evidence that in maternal rubella the virus reaches the developing sensory structures of the fœtus by way of the blood vessels and endolymph.

The striking saccular changes, including thickening and distortion of the walls with adhesions to the macula, suggest that collapse of the saccule may have occurred during the maternal rubella infection.

It is difficult to explain the limitation of the changes to the cochlear duct and saccule. The development of the utricle and canals is complete before that of the cochlea and the fluid systems of the two portions may be separate during the attack of the rubella on the developing cochlear portion. This does not explain the similar pathological findings in postnatal lesions.

The lesions are presumably produced by a blood-borne toxin or virus and as the stria vascularis has the best blood supply of all the structures in the membranous labyrinth the endolymph of the affected areas might contain a higher concentration of the irritant and this would explain a predilection for damage to saccule and cochlea. Fluid movement through the utricular duct is necessarily slow on account of the narrowness of its lumen (0·1 mm. diameter) and dilution of the toxins might well occur rapidly enough to render them innocuous in the utricle and canals. It is also possible that the utriculo-endolymphatic valve effectively isolates the utricle and semicircular canals from the cochlear portion of the labyrinth.

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Dr. L. Fisch:

Congenital Deafness Associated with Hæmolytic Disease of the Newborn

Dr. Fisch gave the results of an investigation carried out with Dr. D. A. Osborn of the Department of Pathology of the Institute of Laryngology and Otology. This investigation concerned 30 cases which had been seen from 1951 to 1953. These 30 cases were divided into two groups. The first showed a rather moderate loss of hearing for high frequencies, and the other group showed severe loss of hearing for high frequencies. By means of slides he illustrated the various characteristics of the deafness in both these categories.

He attached great importance to the study of the neurological complications. According to the findings of the investigators there was a relation between the degree of neurological complications and the degree of deafness.

As for the mental condition, only one mentally deficient and one dull child was found among these 30 cases. Again and again they got cases at their clinic of children who had been previously stated to be mental defectives. They came up with deafness which had not been suspected and only after their arrival at the clinic was it found that these children were actually mentally normal but very deaf.

The conclusions reached as a result of the investigation were both theoretical and practical. The most important practical conclusion was that all children who survived after hæmolytic disease should have detailed hearing tests. He added that it was not easy to test these children and that it was often necessary to refer them to a special clinic for the purpose.

The full results of the investigation appear in (1954) *Arch. Dis. Childh.*, **29**, 309.

[*May* 7, 1954]

Observations on the Circulation of the Cochlea [*Abstract*][1]

By J. C. SEYMOUR, M.B., B.S.

(*From the Ferens Institute, Middlesex Hospital, London*)

THE present concepts on the physiological behaviour of the cochlear vessels and their response to vasoactive drugs are based on indirect experimental findings. For a number of reasons these methods are unsatisfactory and hence the results are not entirely beyond question. The cochlear vessels are said to behave in a "paradoxical" manner with adrenaline and histamine but in these investigations, where every effort has been made to maintain the conditions in as physiological a state as possible and the methods have been indirect as well as direct observation of the living cochlear vessels, the response has been noted to be a normal one. Adrenaline in dilutions of 1/10,000 produces constriction of the terminal arterioles, metarterioles and precapillary sphincters, followed by a secondary vasodilatation.

Histamine produces dilatation of the terminal arterioles and metarterioles but the precapillary sphincters continue to function in a physiological manner unless damaged by excessive concentrations of the drug. An important therapeutic point to be considered is the choice of vasodilator drug to be used. One which causes widespread vasodilatation may, in fact, reduce circulation in "non-essential" capillary fields, by lowering the pressure or by the reflex vasoconstriction which occurs in an attempt

[1]See *J. Laryng.* (1954), **68**, 689.

to prevent fall of pressure. The circulation in the capillary network of the stria vascularis is very largely independent of that in the remainder of the spiral ligament and is itself continuous from apex to base of the cochlea. The speed of circulation in this network is slower than that in the capillaries of the ligament, enabling the maximum metabolic exchanges between the blood and the endolymph to take place.

The production of the endolymph itself occurs at a number of sites other than the stria vascularis. It is said to be produced in the regions of the maculæ of the sacculus and utriculus and the cristæ of the semicircular canals. From a study of a large number of congenitally abnormal, fœtal and normal histological material a number of facts have been adduced. The stria vascularis, in order to produce enough endolymph to fill out the scala media, must be normally vascularized. In congenital deaf-mutism where endolymph is present in the utricle semicircular canals and saccus endolymphaticus but absent in the scala media, vascularization of the stria vascularis is seen to have failed. In rubella cases in which there is early interference with the vascularization of the stria a similar histological appearance is seen.

Although it is believed that there is a slow endolymph current towards the saccus endolymphaticus and that absorption occurs in it, histological examination of the walls indicates quite the contrary point of view. There appear to be at least four types of secretion contributing to the endolymph in the saccus. Two types are provided from specialized papillæ, some of which have a capillary network in their cores and others have non-vascular cores. From these papillæ, as at other sites, cells may be seen to liberate their contents into the endolymph and to float off into the lumen of the saccus where they break up. The third variety of secretion is formed by the extrusion of globules of secretion at the free border of the living cells. The fourth contribution may be produced from the rich capillary network around the saccus but especially at its distal end. The peculiar composition of the endolymph supports this view, especially the fact that its potassium content is twenty to thirty times that of perilymph, suggesting that it is formed largely of the cytoplasm from living cells.

These views are not in agreement with the belief that the saccus absorbs endolymph but they do explain the histological findings and other observations such as the presence of endolymph in the saccus in deaf-mutism. The utriculo-endolymphatic valve prevents reflux of endolymph from the utricle and since the stria and saccular macula are not developed in these cases there is no endolymph secretion in the scala media and sacculus, hence the presence of endolymph in the saccus suggests that secretion takes place in it.

In the light of these findings, which are at variance with present concepts, a number of considerations are offered in explanation of some otological disorders, the most important of which is a reconsideration of the "vascular factor".

Psychogenic Deafness [*Abstract*][1]

By Wing Commander P. F. KING, F.R.C.S.Ed., D.L.O.

(*From the Department of Otorhinolaryngology, Central Medical Establishment, Royal Air Force, London*)

PSYCHOGENIC deafness is a convenient term which conveys no clear-cut picture of any aural disorder. It may be classified as follows:

(1) *Functional deafness.*—(*a*) Loss of discrimination faculty (Kopetzky); (*b*) organic deafness with hysterical overlay, and (*c*) pure hysterical deafness with no evidence of organic defect.

(2) *Malingering.*—(*a*) Malingering associated with hysteria; (*b*) malingering with organic defect; and (*c*) simple malingering.

Loss of the capacity for discriminative listening.—This occurs in patients in the older age groups, in deaf children, and in deaf adults who have not been rehabilitated by an aid or lip-reading. I have seen 9 cases in young male adults employed on responsible "listening" jobs in telecommunication—in all the hearing was normal.

Functional deafness.—Chubb (1946) gave a good definition: "Cases of hysterical deafness have on the one hand no organic lesion to account for the deafness, and on the other no *conscious* responsibility for the deafness present. They have nothing in common with the deliberate malingerer except the absence of an organic lesion." The incidence of the condition is unknown and the frequency with which it is said to occur under combat conditions varies from one writer to another.

Hysterical deafness may occur alone or be associated with organic deafness, and 12 cases of the latter nature were seen. In addition in 19 cases of pure functional deafness there was a history of some form of aural disease in 12. Both types occur in those of low mentality, poor education and ebbing morale.

The detection of functional deafness.—This may be difficult if an organic deafness has a hysterical overlay. Unilateral deafness is commoner than bilateral deafness, except in cases of organic deafness with hysterical overlay.

[1]See *J. Laryng.* (1954), **68**, 623.

A history of sudden onset of hearing loss should be suspect, and the demeanour of the patient may help. The response to whisper and tuning fork tests may show divergent results. The patient with hysterical deafness reacts as though his hearing loss is real, and because of this reaction ordinary tests for proving malingering are not very helpful.

The use of audiometric tests.—Doerfler and Stewart (1946) found that consistency of response on successive audiometric tests was not necessarily always indicative of organic deafness. They found it in patients with functional deafness and assumed that the patient employs a figurative yardstick against which *all* sounds are gauged.

We employ ascending and descending scales of intensity in testing with pure tone audiometry and these generally show divergent findings on the first test.

The efficiency test is of use; in this the subject listens to recorded speech at an intensity of 106 decibels in a background noise of 100 decibels. The scores obtained are far below those of patients with the most advanced form of perceptive loss. This corresponds with the finding of Doerfler and Stewart, namely, that when noise is introduced in measured quantity into a system where speech is already present the patient with psychogenic deafness responds in a different manner from the patient with normal hearing or one with organic loss.

Psycho-galvanic tests have been used by other writers.

The value of tests of labyrinthine function.—The value of these tests is debatable; a normal response is not necessarily evidence of hysterical deafness.

Management.—Early diagnosis is imperative. Early suggestion may be started by the otologist, the later care should be by the psychiatrist. The use of the Pentothal abreaction is advocated. During the abreaction the psychiatrist may get an insight into what has precipitated the deafness. Suggestion can be attempted in the period of recovery. [Three typical cases were described.]

Malingering.—This occurs as an entity, but is also associated with organic deafness and sometimes with hysteria. Generally unilateral deafness will be simulated, as the pretence is easier to maintain; there may be an associated self-induced otitis externa. Lombard's test and repeated audiometry are favoured in detecting the malingerer.

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JOINT SUMMER MEETING WITH THE SECTION OF LARYNGOLOGY HELD AT THE SCARBOROUGH HOSPITAL, SCALBY ROAD, SCARBOROUGH

OTOLOGICAL SESSION

[*June* 10, 1954]

Chairman—R. R. SIMPSON, F.R.C.S.Ed.
(President of the Section of Otology)

The Pathology of Otitis Media—Experimental and Human [*Abstract*][1]

By I. FRIEDMANN, M.D.

(*The Institute of Laryngology and Otology, University of London and the Royal National Throat, Nose and Ear Hospital, London*)

THE main purpose of the present investigations has been to compare the pathology of otitis media as observed in present-day material with that described in the pre-penicillin era; and in particular to try to find an answer to some questions frequently raised in connexion with the antibiotic treatment of otitis media—suggesting that the virulence of the principal causative organisms has decreased; or that the pathology of otitis media has changed since the advent of the antibiotics.

The investigations have been conducted on two parallel lines:

(1) The study of the experimental pathology of otitis caused in guinea-pigs by means of intra-aural injections of cultures of the principal causative organisms.

(2) The systematic routine bacteriological and histo-pathological investigation of bone chips from recent mastoid operations.

[1]Full paper to appear in *J. Laryng.* (1954).

Experimental Otitis

No. of guinea-pigs, 266. No. of organisms tested: 37 strains.

RESULTS

D. pneumoniæ (7 strains). The majority of the strains tested proved to be virulent, frequently causing meningitis and spontaneous death of the animal within two to three weeks.

Streptococcus beta hæmolyticus (10 strains). Only an occasional strain caused otitis in a few animals. The course of the disease on the whole was milder than in pneumococcal otitis and spontaneous death of animals was not observed.

Staphylococcus aureus (5 strains). This was as inconsistent in its effect as *Streptococcus beta hæmolyticus*. Only 2 of the strains tested produced otitis in some animals.

Staphylococcus albus (2 strains). Negative.

BCG (4 strains). Occasionally produced chronic lesions.

Monilia albicans (1 strain originally isolated from a case of bronchial moniliasis). This caused suppurative otitis in guinea-pigs.

Ps. pyocyanea (5 strains), and *B. proteus* (3 strains). These were most consistent in their action causing acute suppurative otitis media followed by the development of chronic otitis media leading to osteoplastic obliteration of the cavities of the ear.

SUMMARY

The development and character of otitis media in the guinea-pig depended largely on the infecting organism and followed various courses:

(*a*) Acute suppurative otitis (complicated by meningitis in pneumococcal infections).

(*b*) Acute suppurative otitis subsiding soon but followed by chronic otitis.

(*c*) Chronic otitis developing in a more insidious way after initial latent period.

The fundamental histopathological features observed were comparable with the findings of earlier authors. In contrast with Haymann's (1912, 1913, 1914*a*, *b*) and Wirth's (1935) findings, however, streptococcal infections proved to be milder. Haymann reported that 7 of 11 guinea-pigs infected with hæmolytic streptococci died within fourteen days.

The infection started in the mucous membrane normally lining the middle ear (bulla), the flattened cells of which often revert to a columnar type during the course of the inflammation.

Hypertrophy of the mucosa and osteoplastic obliteration of the ear appeared to be the result, not the cause, of chronic infection in the ear of the guinea-pig. It is suggested that in man also hyperplasia of the mucosa and the arrest of pneumatization need not necessarily precede the development of chronic infections of the middle-ear cleft.

Human otitis media.—The bacteriological and histopathological findings in 215 cases of operated otitis media have been studied. There was no evidence to support the suggestion that the pathology of otitis media had undergone any fundamental change in recent years when compared with Stewart's classical description of the histopathology of mastoiditis (1928).

Cholesteatoma.—The development of *aural cholesteatoma* in experimental otitis of the guinea-pig was also studied.

Migration of stratified squamous epithelium from the external meatus or drum into the bulla and squamous metaplasia of the epithelial lining of the bulla were often observed. This led to the formation of "typical" aural cholesteatoma. No cholesterol deposits of the type described by Simpson (1954) have so far been found in experimental otitis. The term "cholesterol granuloma" is suggested for these structures consisting of deposits of cholesterol crystals surrounded by inflammatory granulation tissue.

Antibiotic treatment of experimental otitis media.—Attempts at the antibiotic treatment of otitis with various antibiotics indicated that pyocyanea infections were as resistant to antibiotic treatment in the guinea-pig as in man.

My thanks are due to Professor F. C. Ormerod and the surgical staff, and to Dr. T. V. L. Crichlow and the staff of the Department of Radiology of the Royal National Throat, Nose and Ear Hospital, for their co-operation and interest.

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Factors Which Influence the Hearing Result in the Surgery of Chronic Otitis Media [*Abstract*][1]

By Ian B. Thorburn, F.R.C.S.Ed.

This paper is based upon a study of 188 radical and modified radical mastoid operations (94 in each group) over a seven-year period 1947 to 1953 inclusive. The cases are divided into six groups, 4 modified and 2 radical, according to the extent of surgery required to control the disease. An attempt was made in each modified case to define within the tympanum a borderline between disease and local limiting tissue reaction.

In *Modified* 1 and 2, after clearing all mastoid disease the tympanum is uncovered by taking down the posterior meatal wall and removing the "bridge" and outer attic wall. The tympanum is not disturbed and a thin tympanomeatal skin flap is turned back.

Modified 1 are cases of acute or subacute infection in which a cortical mastoidectomy would not suffice to control the disease. In *Modified* 2 one is dealing with chronic infection or cholesteatoma, but one is able to recognize and respect a limiting tissue barrier between the disease and the tympanum.

In *Modified* 3 it is necessary to remove the incus and head of malleus to get beyond the disease, usually cholesteatoma.

In *Modified* 4 the incus and whole of malleus are removed but an attempt is made, using the remnants of the drum and meatal skin, to form a closed potentially mobile drum or, at least, to cover the round window.

Radical 1 is a classical radical mastoid operation but the mucosa over the medial tympanic wall is conserved.

Radical 2 is Lempert's mastoido-tympanectomy operation.

The hearing of patients before and after operation is recorded on a practical clinical basis as normal, good, fair, poor or useless. Each group is analysed with regard to the hearing results, the duration and type of disease—whether subacute or chronic infection and the presence of cholesteatoma.

Comparative hearing tables are presented for the combined modified and radical groups and analysed with regard to factors which seem to have influenced the hearing result. Of the modified cases which retained useful hearing (fair, good or normal) 87% remained healed; 71% had mobile tympanic membranes; 48% were in cases with original cholesteatoma. Corresponding figures for modified cases with poor or useless hearing post-operatively are 68%, 20% and 54% respectively.

Only 8 out of 94 radical cases had useful hearing; it is of interest that all of these were healed and in 6 of them a new mobile false tympanic membrane had formed.

Discussion

It is suggested that cases can be divided pre-operatively so far as hearing prospects are concerned into those which are practically hopeless and those which are at least hopeful.

In the hopeless class are all cases with such extensive destruction of the tympanum that a truly radical operation is needed, especially if there is already associated cochlear degeneration.

The hopeful class comprises:

(1) All cases with useful pre-operative hearing.

(2) Most children, especially if so young that one cannot properly assess their hearing.

(3) All cases with a recent acute or subacute exacerbation.

(4) Cases with a large aural polyp, but with good bone conduction.

The writer reduces his personal outlook with regard to surgical treatment of the hopeful cases to the following observations:

(1) The technique employed must make it easy for instrumentation always to be under direct visual control. The use of *magnification* is of substantial advantage, especially in the tympanic region. The writer uses Lempert's technique with some personal modifications.

(2) *Early surgical intervention* is justified in selected cases, especially of cholesteatoma, with a view to conserving hearing. This applies even where the ear in question is the only ear with useful hearing.

(3) *A local tissue reaction* commonly can be recognized within the tympanum limiting the spread of disease. If this is respected it can later become converted into a healed mobile false tympanic membrane.

(4) Actual or potential *blind pockets* in tympanum or mastoid must be avoided. Accordingly a cortical mastoid operation is wrong treatment for chronic middle-ear disease, a modified radical operation being preferred.

(5) The ideal to be aimed at is the creation of a mobile actual or false tympanic membrane in functional continuity with the eustachian tube covering one or both labyrinth windows. If there is no incus or malleus an intact stapes is an asset especially if the mobile drum covers and is adherent to it.

(6) Tympano-plastic operations. Given an ear securely healed with good cochlear function but with a perforated, fixed or absent drum, the observations reported in this paper suggest that the restoration of the tympanum to a closed mobile state should be to the advantage of the hearing.

[1]See *J. Laryng.* (1954) **68**, 739.

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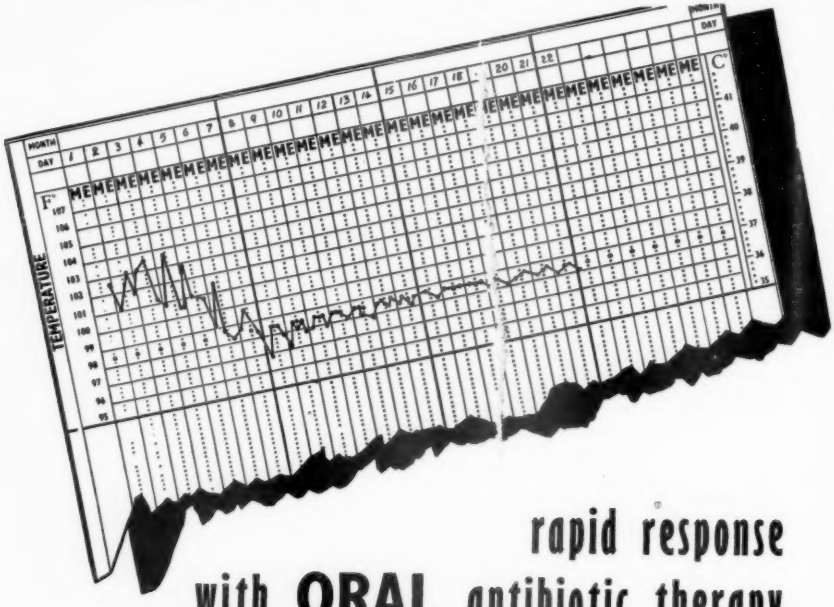

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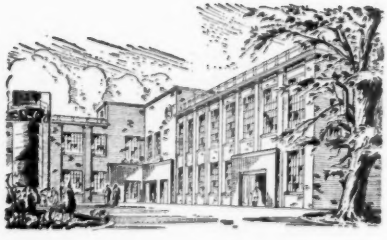

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Section of Laryngology

President—C. P. Wilson, C.V.O., F.R.C.S.

[*May* 7, 1954]

DISCUSSION ON THE MANAGEMENT OF HÆMORRHAGE FOLLOWING TONSILLECTOMY

Mr. D. Walker Ashcroft: During the last few weeks I, personally, have heard of six deaths due to hæmorrhage following tonsillectomy. Of how many more do you know? It seems to me unfortunate that the Registrar-General's Statistical Report does not record the number of deaths due to this cause. A communication from the Statistician of the General Register Office reveals, however, that there were 47 deaths in 1952 in England and Wales attributable in any way to tonsillar or adenoidal hypertrophy. In 42 of these cases the word tonsillectomy appeared on the death certificate. Some of these deaths may have been due to surgical shock or misadventure, or to drug disasters, but I think that these figures at least indicate the existence of a problem. Such hæmorrhage is terrifying enough for the patient but may be equally or even more alarming for the medical man inexperienced in dealing with these cases; it may happen with any patient, or with any operator, however reputable he may be. Its control may demand more knowledge and skill than that required for the performance of the operation itself.

Hæmorrhage following tonsillectomy may be of three types:

(1) *Reactionary hæmorrhage*—or hæmorrhage occurring within the first twenty-four hours after operation.

(2) *Hæmorrhage during convalescence.*—This occurs most commonly on the fifth night or sixth day following operation and is associated with the natural separation of the primary slough from the bed of the tonsillar fossa, and with the tendency of ligatures to come away at this time. It is frequently preceded by a slight rise of temperature but may occur without any post-operative pyrexia.

(3) *True secondary hæmorrhage.*—This differs essentially from the type just mentioned in that it is associated with damage to the muscular tissue of the tonsillar bed and is due to sepsis which results in the sloughing of a blood vessel wall. Examination of the throat in these cases usually reveals considerable redness and œdema of the faucial pillars and uvula, and sometimes an offensive slough in the tonsillar fossa. The local inflammatory reaction is reflected in the patient's temperature chart. True secondary hæmorrhage may occur at any time from the third to the fourteenth post-operative day.

Factors Influencing the Occurrence of Hæmorrhage Following Tonsillectomy

(*a*) Pre-operative.
(*b*) Operative.
(*c*) Post-operative.

(*a*) *Pre-operative*

Although tonsillectomy may be indicated in a particular case certain precautions must be taken before operation is decided upon and many factors must be considered before the actual time of the operation is arranged.

In taking a history of the case, and during examination of the patient, particular attention should be paid to the following points.

(i) *The type of patient.*—Note the physical characteristics of the patient. The subjects of hypertension show a tendency to bleed excessively following operation. In patients of plethoric type, with short thick necks, hæmorrhage is prone to occur. Heavy smokers, chronic alcoholics, and patients with highly excitable and emotionally unstable temperaments also suffer in this respect. Red-headed females are suspect, and the same applies to all sandy-haired, freckly children.

(ii) *Bleeding.*—Most careful enquiry should be made as to whether there is any susceptibility to prolonged bleeding following cuts or abrasions on the part of the patient or any member of his family. It is extremely disconcerting to be informed, after the occurrence of post-tonsillectomy hæmorrhage, that the patient had to be transfused following a previous dental extraction. A history of such bleeding must suggest a blood dyscrasia and demands a complete hæmatological investigation.

The influence on post-operative hæmorrhage of conditions such as severe anæmia or salicylate-induced hypoprothrombinæmia is discussed by Dr. J. W. Stewart.

From the surgeon's point of view tonsillectomy should not be undertaken in such cases until the patient's blood picture can be brought within normal limits.

(iii) *Severe tonsillitis or peritonsillar abscess.*—Recent acute local infections increase the risk of bleeding both during and after operation. For this reason operation should not be undertaken within a period of some weeks after either of these conditions. No hard and fast rule can be laid down but I am of the opinion that, following an acute throat condition, operation should be deferred, if possible, for three to four weeks in a child, and six weeks in an adult.

(iv) *Infections of the nose and accessory nasal sinuses.*—Acute sinusitis, whether associated with a sore throat or not, is a contra-indication to the immediate performance of the operation. A common cold comes under the same category. The presence of chronic sinusitis should not be overlooked and adequate measures for its efficient treatment should be instituted before tonsillectomy.

(v) *Jaundice.*—The fibrinogen content of the liver is extremely low in all destructive hepatic lesions and consequently tonsillectomy is contra-indicated in the presence of jaundice due to any cause.

(vi) *Menstruation.*—On account of the psychological upset in many cases and the delayed coagulation time of the blood, operation should be avoided just before or during the first few days of a menstrual period.

(vii) *Toxic conditions.*—In the case of patients suffering from thyrotoxicosis, nephritis, acute rheumatism and diabetes, the whole problem should be discussed with a competent physician before operation is undertaken. This applies also to diphtheria carriers.

(viii) *Pyrexia.*—It should be an invariable rule not to operate on any patient who has a temperature of 99·0° F., or over, on the day of operation.

(ix) *Stomatological conditions.*—Tonsillectomy should not be performed in the presence of gingivitis, buccal ulceration, or significant dental caries.

(x) *Weather.*—It is generally accepted that tonsillectomy cases tend to bleed excessively if operation is performed during a heat-wave.

(*b*) *Operative*

Consideration of the various methods of tonsillectomy does not come within the scope of this paper. Nevertheless, the skill and care exercised by the operator does influence the incidence of post-operative hæmorrhage. Excessive surgical trauma is always to be deplored. Abnormally large, or aberrant, blood vessels should be seen or felt, and a fatality should never occur due to their severance.

Whatever method of operation is employed, it is imperative that hæmostasis should be efficient. It is far better to spend all the time that is necessary to achieve this end while the patient is still on the operating table, than to be faced with the danger of post-operative hæmorrhage. *The tonsillar fossæ must be dry before the patient leaves the operating theatre.*

The subsequent maintenance of hæmostasis is influenced by the following factors:

(i) *Anæsthesia.*—Deep anæsthesia produced by any agent results in a fall of blood pressure. Later, when this pressure returns to normal, bleeding may recommence owing to separation of clot from the mouth of a blood vessel divided, but overlooked, at the time of operation. Artificially induced hypotension may prove a temporary delight for the operator, but his joy may be short lived!

I think it is desirable that the patient's cough reflex should return almost immediately after the end of the operation.

(ii) *Imperfect clot formation.*—This is most likely to occur in the larger veins in the bed of the tonsillar fossa especially the para-tonsillar vein of Denis Browne. If a vein has been "button-holed", but not completely divided, any obstruction to respiration may cause dilatation of the vein and consequent instability of the clot. Complete division of a large longitudinal vein results in continuous bleeding from its upper end at the time of operation, and for this reason the upper end is usually ligatured. The lower end, however, is collapsed and its contained clot is small. Subsequent dilatation of this lower end renders the clot unstable and hæmorrhage is likely to recur. It is important, therefore, to search for, and tie, the lower end of a completely severed longitudinal vein.

(iii) *Ligatures.*—The slipping of insecurely tied ligatures may be responsible for the occurrence of post-operative hæmorrhage. It is important that the precise bleeding point should be ligatured; if too much tissue is picked up by the hæmostatic forceps, the subsequently applied ligature may slip, or it may cause tearing of the offending blood vessel immediately above or below the site of the original bleeding point. Further, the inclusion of excess tissue in a ligature may lead to local necrosis and sloughing and ultimately to true secondary hæmorrhage.

Reef knots are always preferable to fancy slip knots.

(iv) *Artificial means employed to control bleeding at operation.*—These include the use of vaso-constricting agents and coagulants. The employment of the former group—for example, adrenaline hydrochloride—is not to be recommended at the time of operation because subsequent reactionary vasodilatation occurs and may result in capillary oozing. The same objection does not apply to the latter group which includes purely coagulating agents such as friar's balsam, Protargol, hæmostatic serum, snake-venom and thrombin.

(c) *Post-operative*

Obstruction to respiration is probably the second most important factor in the production of post-tonsillectomy hæmorrhage. It should not occur in the operating theatre; if it does it is a reflection on the competence of the surgeon-anæsthetist team.

At the end of the operation, all blood clot should be removed from the nose and naso-pharynx and an artificial airway inserted in the mouth. Normal unaided rhythmic respiration should be established before the patient leaves the theatre.

On the journey back to the ward the patient should be in the lateral position and should be in the care of some person fully capable of dealing with a backward fallen tongue especially in the presence of a tightly clenched jaw. The maintenance of a clear airway is of the utmost importance following tonsillectomy. Cyanosis always demands prompt action: if it is present, in the absence of a backward fallen tongue or laryngeal spasm, I believe that bronchoscopic aspiration of inhaled blood or blood clot becomes imperative.

After the patient has returned to the ward care must be taken to avoid anything which will tend to produce congestion.

The following measures are calculated to minimize the risk of post-operative hæmorrhage:

(i) The patient is placed in bed in the "tonsil position". This position allows of free respiration and consequently minimizes congestion. It also permits any blood which may collect to run out of the nose and mouth and so be seen rather than remain concealed. Further, the risk of inhalation of blood or blood clot—the most serious cause of respiratory obstruction—is reduced.

(ii) The artificial airway should be removed when the patient discards it—provided that the cough reflex has returned.

(iii) If the patient becomes restless soon after operation, and provided there is no bleeding, a sedative should be given. For adults, 1/6 grain Omnopon is recommended, and for children, Nepenthe or papaveretum, in standard dosage, is useful.

(iv) The diet should be restricted to cold fluids or semi-solid food for the first twenty-four hours.

(v) The patient should be confined to bed for the first post-operative day. After that he may be allowed up for essential purposes, and may remain out of bed for a period during the next three days. I do not insist that a patient should be confined to his bed for a week following tonsillectomy. I believe that the struggle involved in balancing precariously on a bed-pan may do more to cause a rise of blood pressure than the peaceful use of a bedside commode or a near-by lavatory.

(vi) Hot baths are inadvisable for the first week following operation. For the next week warm baths are allowed.

(vii) The patient leaves hospital at the end of a week. During the next week he should avoid strenuous exercise, alcohol and smoking. He should endeavour, also, to avoid developing an upper respiratory tract infection, which might be contracted by his going to a theatre or cinema—or even to church.

(viii) The post-operative use of salicylates is deserving of mention. Some investigators have sought to attribute to the widespread post-operative use of Aspergum a rate of late tonsillar hæmorrhage of the order of 10%, due to salicylate-induced hypoprothrombinæmia. Other observers, however, assert that salicylates, even when given in massive doses, do not cause a fall of the blood prothrombin level sufficient to create a hæmorrhagic diathesis. There is no unanimity of opinion on this question at present. Personally, I have yet to experience any untoward effects due to the use of aspirin mucilage (10 grains to 1 oz.), whereas I am convinced of the comfort it affords the recently tonsillectomized patient.

The Management of a Case of Hæmorrhage

(a) *Reactionary Hæmorrhage*

Slight oozing, which should be of insignificant amount, usually occurs during the first hour after operation but ceases at the end of this time in the vast majority of cases. If free oozing occurs after the first hour, or if there is vomiting of freshly swallowed blood, the patient must be considered to be suffering from reactionary hæmorrhage. This is treated according to the following routine procedure:

If a sedative has not been needed, or has not been given already, one should be given now. For this purpose there is no more efficient preparation than morphine hydrochloride which not only lowers the blood pressure but also diminishes the tendency to early post-operative vomiting. I am of the opinion that, in the case of adults, an initial dose of $\frac{1}{4}$ grain administered hypodermically is far more effective than a dose of 1/6 grain repeated at the end of half an hour. For children, subcutaneous papaveretum or Nepenthe is admirable.

Unless the hæmorrhage is so free as to necessitate urgent attention it is now wise to wait for twenty to thirty minutes before examining the throat. At the end of this time the examination is usually accomplished without difficulty, for the morphine has minimized pain, diminished the throat reflexes, and allayed to some extent the nervous anxiety of the patient.

Whenever morphine or one of its derivatives has been given, the *tonsillar fossæ must be inspected* half an hour after the administration of the drug. The surgeon should make this examination himself, and not rely on the report of possibly indifferent observers. Careful search must be made to detect any oozing or trickling from the fossæ, for, although a nurse may say that there has been no further bleeding, the patient may still be swallowing blood. This may accumulate slowly in the stomach to such an extent that the pulse-rate may rise alarmingly immediately after a pint of blood has been vomited.

It is not uncommon for a patient to go to sleep after morphine has been given and then, a couple of hours later, suddenly to waken and vomit a large quantity of blood.

Details of examination and treatment.—A good source of illumination is essential for this examination, and in order to leave both hands free a head-lamp or head-mirror should be employed. If it is thought that hæmorrhage is still continuing, the patient—who is in a propped-up position—is given a tumblerful of cold water, and is asked to rinse out the mouth three or four times. The rinsings are voided into a basin. A final mouthful is then taken and swallowed. This renders the mouth fairly free from blood and facilitates inspection of the tonsillar fossæ. If on inspection there is no bleeding, further action is unnecessary. If there is bleeding the tongue is depressed gently but firmly by means of a tongue depressor held in one hand and, with an instrument such as Luc's ethmoidal forceps held in the other, *all* blood clot is removed from the offending fossa. Another mouthwash of cold water is then given. Total removal of the clot may be all that is necessary to terminate the bleeding. If hæmorrhage continues, a pledget of cotton-wool, soaked in peroxide of hydrogen and then wrung nearly dry, is inserted into the tonsillar fossa. The tongue depressor is then removed and the patient is allowed to close his mouth on the forceps, the pledget of wool still being pressed into the fossa. At the end of a minute the wool is removed and a fresh but similar pledget applied in the same manner as the first. If necessary, yet a third pledget is applied.

If, at the end of this time hæmorrhage is still occurring, the whole procedure is repeated, substituting thrombin solution for the hydrogen peroxide. These measures usually suffice to control the bleeding. Other agents which may be employed in the treatment of reactionary hæmorrhage are:

(i) *Ice.*—The external application of cold to the head and neck may help in some cases by inducing reflex vasoconstriction. I think that the sucking of ice is without value because it promotes repeated swallowing and this is conducive to further bleeding.

(ii) *Clamps.*—If bleeding is brisk it may be controlled temporarily by the application of a suitably padded clamp of the Courtenay Yorke or Watson-Williams design. Clamps should be applied firmly, but not so tightly as to traumatize the tissues between the blades. If possible their use should be avoided altogether, as they are responsible for much discomfort to the patient.

If the measures taken appear to have stopped the bleeding, the patient is allowed to rest for a while in order that the morphine may be given a chance to complete its work. The pulse-rate is recorded at fifteen-minute intervals and a careful watch kept for further signs of hæmorrhage. If hæmorrhage does appear to continue, or if in spite of no apparent bleeding the pulse-rate is rising, the tonsillar fossæ should be inspected again. If the measures enumerated above have not been successful in controlling the bleeding arrangements should be made for the return of the patient to the operating theatre without delay.

I am convinced that it is better to give a second anæsthetic while the patient's general condition is still relatively good than to wait until his state is so precarious that any operative campaign must necessarily prove hazardous to a degree. These remarks apply even more forcibly in the case of children or elderly people who are particularly intolerant of continued hæmorrhage and in whom any unnecessary delay in securing hæmostasis may well prove fatal. A steadily rising pulse-rate, a pulse that is irregular or easily compressible, a cold and clammy skin, cyanosis, shallow and rapid respiration, great restlessness, and the continued vomiting of blood are all danger signs to be avoided rather than treated when they occur.

As soon as a decision has been made to take the patient back to the theatre he is given a hypodermic injection of 1/100 grain of atropine sulphate.

The anæsthetic agent to be employed is a matter of some importance. Some years ago the anæsthetic of choice on this second occasion was "open" ether, which was well tolerated by these exsanguinated and morphinized patients. To-day the position is rather different. Most anæsthetists are agreed that, for adults, a *small* dose of thiopentone (0·25–0·5 gramme) plus a relaxant, followed by nitrous oxide, oxygen and ether delivered through an intratracheal tube, is the ideal sequence. In children, gas, oxygen and ether is the anæsthetic of choice. Induction should be carried out with the patient's head lowered and turned to one side. Aspiration of blood from the nose, post-nasal space and oropharynx may be carried out with a rubber catheter connected to a suction apparatus. On no account should chloroform be administered, for it not only exerts a toxic influence on the myocardium but lowers the blood pressure and consequently conceals hæmorrhage.

A gag is inserted in the mouth and once more all clot is removed from the offending fossa in order to expose the source of the hæmorrhage. Single bleeding points are clamped and ligatured. It may be necessary to under-run a bleeding vessel with a catgut stitch threaded on a small curved needle.

If there is a general ooze a swab soaked in ice acriflavine (1 : 1,000) solution is inserted into the fossa and held there for four minutes by the clock. The local application of thrombin may also prove effective in controlling a general ooze. If this fails to control the oozing a swab moistened in pure turpentine may be tried.

If all the above measures fail, the faucial pillars should be sutured together over a gauze plug or gauze-covered pledget of wool soaked in the acriflavine solution. Two sutures suffice: they, and the plug, are removed after twenty-four hours.

(b) Hæmorrhage During Convalescence

In the vast majority of cases, hæmorrhage of this delayed type occurs on the fifth night following operation. As a rule it is not severe, and may consist only in the patient coughing up a small bright red clot. It usually ceases after a gargle of weak hydrogen peroxide. Sometimes the hæmorrhage, although not severe, continues during the course of an hour or more, and is associated with throat discomfort due to the presence of clot. The patient's efforts to dislodge this clot may then prolong the bleeding, in which case the treatment becomes exactly the same as that already described for reactionary hæmorrhage. It will be found, however, that it is seldom necessary to remove the clot, or to take the patient back to the operating theatre.

(c) True Secondary Hæmorrhage

Hæmorrhage of this type is much more serious than that described under the heading of hæmorrhage during convalescence. Fortunately, it is also more uncommon. When it does occur, there is frequently a small "warning" hæmorrhage on one day followed by a larger one within the next twenty-four hours. In such a case it is likely that the patient will have to be taken back to the theatre. The control of this type of bleeding is often difficult, for it is seldom possible to clamp and ligate a single bleeding point on account of the friability of the sloughing and œdematous tissues of the bed of the tonsillar fossa. If the more simple measures already advocated for the control of bleeding are ineffective, recourse to suturing the faucial pillars will be necessary.

According to the literature, ligation of the external carotid artery is of doubtful efficacy in any type of tonsillar hæmorrhage on account of the extensive anastomosis of this vessel. I have never seen it performed for this purpose.

Blood transfusion may be life-saving in cases of severe hæmorrhage, but it is desirable that effective measures for the control of any bleeding should be instituted before transfusion becomes necessary.

In conclusion, may I repeat that the most important factors in the prevention of post-tonsillectomy hæmorrhage are careful selection of cases suitable and fit for operation, a competent operative technique, complete hæmostasis in the operating theatre, and the maintenance of a free airway until the patient regains complete consciousness. There must be no complacency about this problem and, if hæmorrhage does occur, there must be no procrastination in dealing effectively with this dangerous post-operative complication.

Dr. J. W. Stewart: I propose to limit myself to those cases of tonsillar hæmorrhage in which a coagulation defect can be demonstrated by the laboratory and clinical tests that are available at the present time. This group of cases includes conditions such as hæmophilia and is of great importance clinically as they nearly always bleed profusely and require much careful management in the post-operative period.

In order to attempt rational management of these cases, it is necessary to understand the nature of the defect and the part it plays in blood coagulation. To do this effectively it is desirable to examine the processes by which normal blood coagulates. This is extremely complicated and in some aspects is not completely understood. The present position is summarized as follows:

Blood coagulation

Platelets + anti-hæmophiliac globulin + Christmas factor + Factor VII + Ca^{++}

↓

Thromboplastin

+

Factor V + Prothrombin + Ca^{++}

↓

Thrombin + Fibrinogen

↓

Fibrin

From this it can be seen that blood coagulation takes place in three stages:

First—formation of thromboplastin.

Second—formation of thrombin from prothrombin.

Third—formation of fibrin from fibrinogen.

The formation of thromboplastin from the blood itself—called intrinsic thromboplastin—is now thought to be of much greater importance than the intrinsic thromboplastin which exudes from damaged tissues. All the factors shown above are of vital importance in the coagulation mechanism

and the absence of any one of these will cause a serious delay in blood clotting or in some cases, such as absence of fibrinogen, failure of the blood to clot at all. Each factor, if reduced in amount or absent, can cause a hæmorrhagic disorder and I shall examine each in turn and indicate its importance.

Fibrinogen.—This is of fundamental importance as no clot can be formed without it. Absence of fibrinogen, afibrinogenæmia, is a very rare congenital abnormality. Otherwise fibrinogen is practically never sufficiently reduced during life to interfere seriously with coagulation but deficiency may occur as a terminal event, along with other deficiencies in severe liver diseases and secondary carcinomatosis.

Calcium.—Removal of Ca ions is a standard method of making blood incoagulable for use in laboratory tests. But Ca ions are never so deficient, *in vivo*, to interfere with blood clotting.

Prothrombin.—Lack of prothrombin is an uncommon deficiency but it definitely does occur in a few cases of obstructive jaundice with vitamin-K deficiency. There is also some reduction in patients receiving dicoumarol therapy but it is not the main deficiency which is in Factor VII.

Factor V.—So-called because in 1947 when it was discovered it was the fifth factor known to be necessary for blood coagulation, the others being Ca, fibrinogen, prothrombin and thromboplastin. Deficiency can occur as a congenital defect but is very rare. Acquired deficiency does occur in severe liver diseases and advanced carcinoma. Stefaniri found some reduction after operation which was maximal on the third post-operative day with full recovery on ninth day. But few, if any, cases of post-operative hæmorrhage appear to be due to this.

Factor VII.—This is the seventh factor described, Factor VI being the active form of Factor V. It is of great importance clinically. Deficiency of this factor is the main defect in the coagulation mechanism caused by Tromexan and dicoumarol therapy and it is also deficient in persons who are taking heavy doses of salicylates.

Christmas factor.—Named after the patient who was first discovered to be deficient of this factor. Christmas disease is clinically similar to hæmophilia but the concentration of the anti-hæmophiliac globulin is normal. The distinction is of clinical importance because in Christmas disease stored blood is an efficient corrective, the factor being stable on storage.

Anti-hæmophiliac globulin.—This fraction of the globulin proteins is absent or seriously reduced in cases of hæmophilia. The protein is unstable and stored blood from blood bank is also often deficient in this factor, but it is present in normal fresh blood.

Platelets are very seriously reduced in primary and secondary thrombocytopenia. Blood does clot in their absence but clot is very fragile.

Methods Available for Detecting Coagulation Defect

The tests available in the clinical pathology laboratory for the investigation of a possible hæmorrhagic diathesis are as follows:

(1) *Coagulation time.*—Normal 4–10 min. (Lee and White). This is the oldest and simplest test; it is not very sensitive but is valuable for this very reason, because if it is abnormal coagulation is very defective. It can be normal in some cases of hæmorrhagic diathesis and especially in cases of thrombocytopenic purpura. It should always be performed with a clot retraction test.

(2) *Clot retraction.*—Normal at least 40% liquid expressed after two hours' incubation at 37° C. Clot retraction is often defective in hæmorrhagic diathesis but again it is not very sensitive but better than the coagulation time alone. However, it tends to be normal when the coagulation is normal and, therefore, lets one down when it is most required.

(3) *Platelet count.*—Normal 200,000–500,000 per c.mm. Less than 100,000 or more than 1 million per c.mm. are pathological.

(4) *Bleeding time.*—1–4 min. (Duke). A very crude test, but if abnormal indicates a very serious defect in capillary contractibility.

(5) *Hess's test for capillary fragility.*—A very important test performed quite simply by inflating a sphygmomanometer cuff between systolic and diastolic blood pressure and maintaining for five minutes, at the end of which time the cubital fossa is examined for petechiæ. If more than one or two are present the test is positive and indicates excessive fragility of the capillaries which is *the* abnormality in the purpuras.

(6) *Prothrombin time* (one-stage method—Quick)—This test does not measure prothombin only. It is only normal if prothrombin, Factors V and VII and fibrinogen are normal.

(7) *Prothrombin consumption test*—This test is abnormal in any condition where the formation of thromboplastin is deficient. Timing is very important. This test is not very sensitive but may be abnormal when the coagulation time is normal.

(8) *Thrombin generation test*—A very useful screen test. It enables one to measure the exact amount of thrombin formed during the coagulation process and will therefore indicate a deficient formation of thrombin in all coagulation disorders with the exception of fibrinogenopenia. If found to be

abnormal the use of the thromboplastin generation test, tests for inhibitors or anticoagulants may enable the exact identification of the defect.

The following cases from my own experience illustrate some of these points:

Case I.—A single woman aged 30 sent for pre-operative investigation (? hæmorrhagic diathesis) because she stated that she had once bled for twelve hours after a tooth extraction and had become weak and nearly fainted. No transfusion was required and since then a further two teeth had been extracted without causing any hæmorrhage. This is a most unconvincing history. Most patients who tell a similar tale have nothing wrong with them but any patient giving a history of excessive hæmorrhage should always be fully investigated.

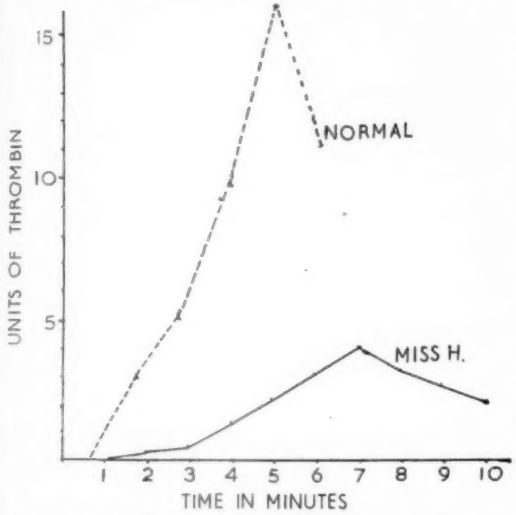

FIG. 1.—Thrombin generation test on plasma of Miss H. compared with normal plasma.

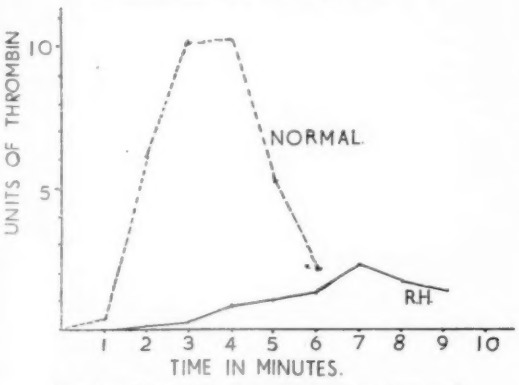

FIG. 2.—Thrombin generation test on plasma of Master R. H. compared with normal plasma.

Miss H., aged 30. Coagulation time 7 minutes. Clot retraction nil. Platelets 45,000 per c.mm. Bleeding time 6 minutes. Hess's test, many petechiæ. Prothrombin time 16 seconds. Prothrombin consumption test 50%. Thrombin generation test, very low thrombin generation (Fig. 1).

In this case the Hess's test and bleeding time are characteristic of the purpuras—and the blood platelets are reduced. Therefore, the case is one of thrombocytopenic purpura. In the purpuras the primary defect is a capillary defect, viz. excessive fragility and failure to contract and stop bleeding. The platelet defect simply adds a coagulation defect to this background. The bleeding can be very severe, welling up from microscopic vessels. There is no macroscopic bleeding point.

Case II.—R. H., boy aged 13. Coagulation time 17 minutes. Clot retraction nil. Platelets 300,000 per c.mm. Bleeding time ½ minute. Hess's test, no petechiæ. Prothrombin time 14 seconds. Prothrombin consumption test 34%. Thrombin generation test, much-reduced thrombin formation (Fig. 2).

The mother stated that he bruised easily and bled profusely from cuts, but there was no history of any definite episode affecting the boy. This patient was referred to the laboratory pre-operatively for ? hæmorrhagic diathesis.

Family history.—? a cousin and an aunt who bleed excessively.

The results of the tests indicate a severe coagulation defect. The abnormal coagulation time and clot retraction test in the presence of a normal prothrombin time (Factors V, VII and prothrombin and fibrinogen normal) indicate that defect must be either in anti-hæmophiliac globulin or Christmas factor or some inhibitor.

Table I indicates the results of tests which correct the two defects in turn.

TABLE I.—R. H.

	Recalcified plasma clotting time
Patient's plasma alone	200 seconds
Patient's plasma + 20% normal plasma	105 seconds
Patient's plasma + 20% normal serum (contains Christmas factor) ..	95 seconds
Patient's plasma + 20% normal plasma $Al(OH_3)$ absorbed	205 seconds
Patient's plasma + 20% fibrinogen factor (contains A.H.G.)	195 seconds
Patient's plasma + 20% hæmophiliac plasma	90 seconds

This indicates clearly that the addition of Christmas factor corrects the coagulation time and therefore the case is one of Christmas disease.

Case III.—B. L., boy aged 3, referred for investigation on account of a melæna. Coagulation time 70 minutes. Clot retraction nil. Platelets 260,000 per c.mm. Bleeding time 1½ minutes. Hess's test negative. Prothrombin time 16 seconds. Prothrombin consumption test 100%. Thrombin generation test, much-reduced thrombin formation (Fig. 3).

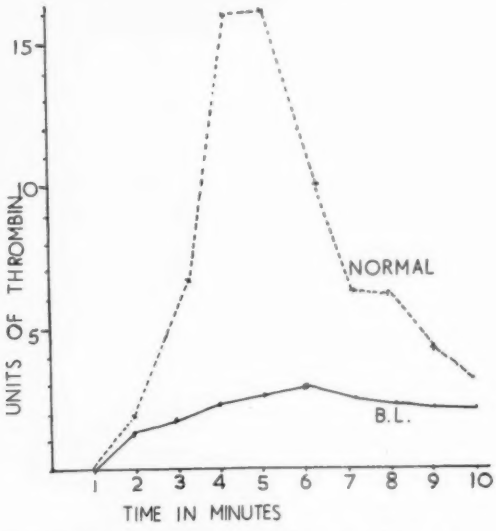

FIG. 3.—Thrombin generation test on plasma of Master B. L. compared with normal plasma.

There was no history of previous bleeding or any family history. In this case again we had the combination of an abnormal coagulation time with a normal prothrombin time and in Table II it will be seen that the coagulation time is corrected by the addition of anti-hæmophiliac globulin.

The laboratory findings in this case are typical in every respect. The clinical history of hæmorrhage from trivial cuts, bruising or slight trauma and hæmarthroses will undoubtedly be obtained when the child grows older. The absence of a family history of "bleeders" in relatives is not uncommon in these days of small families.

TABLE II.—B. L.

	Recalcified plasma clotting time
Patient's plasma alone	385 seconds
Patient's plasma + 10% normal plasma	257 seconds
Patient's plasma + 10% fibrinogen (contains A.H.G.)	198 seconds
Patient's plasma + 10% normal serum (contains Christmas factor. No A.H.G.)	327 seconds
Patient's plasma + 10% hæmophiliac plasma	340 seconds

Case IV.—Man, aged 60. He gave a history of being discharged from the Army forty years ago as a "bleeder" following an accident. He recently had had several hæmatemeses from a peptic ulcer but there was no other history of hæmorrhage. The investigations showed a defect in the blood clotting time but a normal bleeding time.

Mr. M. Coagulation time 10 minutes. Clot retraction 10%. Platelets 290,000 per c.mm. Bleeding time 0 minutes. Hess's test, no petechiæ. Prothrombin time 13 seconds. Prothrombin consumption test 55%.

In fact this patient is a hæmophiliac and his daughters' two sons are known hæmophiliacs, so that in this instance the family history is typical.

It is always preferable to have such patients investigated pre-operatively in order to discover the defect beforehand.

In all these cases the hæmorrhagic condition was demonstrated pre-operatively and if operation is absolutely necessary they may be operated on. The corrections of the coagulation time with serum, fresh blood, &c., are indicated by the laboratory tests. These patients if operated on will need daily infusion of plasma for at least two weeks and in amounts up to 2 litres daily. Operation very definitely carries an increased risk to life and although the defect is to some extent corrected by transfusion therapy the patient cannot be considered normal and wound healing is always slower than normal.

In cases in which the condition is discovered after operation it cannot be too strongly emphasized

that the stake is no less than the patient's life and treatment with blood transfusion must be instituted without delay. In the modern hospital with an efficient and well-organized transfusion service, no patient should die of hæmorrhagic anæmia. Blood and plasma are available and should be used and will have to be used for some fourteen days. Death is more likely to be due to effects of excessive hæmorrhage, such as inhalation of blood. In any case in which bleeding is excessive care should be taken to see that the patient is kept in such a position that blood runs out of the mouth and is not swallowed. This also allows a more correct estimation of the amount of blood lost which is often underestimated in those cases in which it is swallowed.

Mr. Stirk Adams referred to the observation by Mr. Ashcroft in his opening paper that some surgeons felt that post-tonsillectomy hæmorrhage was not a problem, but in his experience in the Children's Hospital, Birmingham, where a large number of operations were performed, this complication was frequently encountered, and its incidence during the past year had been investigated. In a total of 2,041 operations there were 66 cases with varying degrees of reactionary post-operative hæmorrhage; in 42 of these this was of minor severity, in 11 intermediate and in 13 a continuing hæmorrhage occurred which needed transfusion for its control.

In this hospital there were two separate operating services, one for in-patients using premedication and a dissection and ligature technique; and the other a day-ward service, with atropine premedication, a short anæsthesia, usually ethyl chloride, and a guillotine operation (Table I).

TABLE I.—THE MONTHLY RECORD FOR EACH SERVICE

Month	In-patients	Hæmorrhage	Transfusion	Day-ward patients	Hæmorrhage	Transfusion	Total hæmorrhage
1953							
May	18	1	—	125	4	1	5
June	23	1	—	84	3	—	4
July	27	1	—	100	None	—	1
Aug.	46	5	—	100	2	1	7
Sept.	38	3	1	173	2	—	5
Oct.	64	4	—	146	None	—	4
Nov.	59	6	1	103	3	—	9
Dec.	48	2	2	154	2	1	4
1954							
Jan.	47	5	—	104	3	2	8
Feb.	51	2	1	134	3	1	5
Mar.	63	3	1	156	4	—	7
Apl.	60	3	—	118	4	1	7
Totals	544	36	6	1,497	30	7	66

Their practice when continuing hæmorrhage occurred was to carry out a blood cross-matching early and transfusion was the usual method of treatment, as it had been found that 6 oz. of whole blood was the most effective measure in its control.

The survey showed that the risk of a post-operative hæmorrhage after the dissection operation was three times greater than after the guillotine operation and although cases for both series are selected with a high proportion of tonsillar reticulo-fibrosis in the in-patients, the disproportion between the risk in these groups suggested that the barbiturate premedication, the longer anæsthetic, and the slower post-operative recovery were factors increasing the risk of post-operative hæmorrhage.

Another significant finding was the variation in seasonal incidence and it was of interest that no case required a transfusion between May 5 and August 18, 1953. He felt there was a close connexion between the waves of upper respiratory infections with their five-weekly periodicity during the autumn and the rising incidence of post-operative hæmorrhage, and this had led to the development of the thesis that the epidemics of upper respiratory infections interfered with the clotting capacity of these patients, although at the time they had no history and showed no physical signs of reaction to an upper respiratory infection.

Mr. Stuart Mawson considered that, apart from stopping the bleeding, the importance of the maintenance of blood volume should be emphasized. The volume that could be safely lost without replacement depended on the age of the patient, and was equivalent to about one-tenth of his total blood volume. This in a child aged 2 years amounted to only half a teacupful (100 ml.) whereas an adult could safely lose a whole bottleful (500 ml.); if two-tenths of the blood volume were lost the "alert" must be sounded, though replacement might not prove necessary, but if three-tenths of the blood volume were lost, replacement was urgently required. If matched blood were not immediately available a substitute, such as dextran, was appropriate in an acute hæmorrhage. The fact that a rising pulse-rate and restlessness did not always indicate bleeding (in a recent case it had been found due to post-anæsthetic ketosis) added further point to the necessity for careful measurement of all blood lost during and after operation.

Mr. A. Bowen-Davies said that he thought the speakers had suggested giving a second anæsthetic for the arrest of hæmorrhage in a rather light-hearted manner. He considered it to be a very dangerous procedure and only to be employed when absolutely necessary. The case should then be in the hands of an expert anæsthetist and surgeon.

Mr. R. G. Macbeth said that about twelve years ago they had had the benefit of a discussion with a hæmatologist on much the same topic as that of to-day (*Proceedings*, 1942, **35**, 401). He had asked two questions then and wished to repeat them. Firstly was there anything in the theory that red-haired people tended to bleed more than others? Secondly did menstruating women bleed more at tonsillectomy? On the previous occasion the answer to both questions had been in the negative, and his own impressions supported those views. He thought the red-haired story was nonsense and that menstruation should be disregarded.

With regard to the seasonal incidence of bleeding, it seemed possible that children tended to bleed more during the occasional heat-wave met in this country. If it became necessary to take a child back to the theatre in those circumstances, a second dose of atropine should not be given, because of the adverse effect of this drug upon the heat-regulating mechanism of the body. This might be dangerous even to the point of death.

Mr. R. S. Strang said that on the treatment of reactionary hæmorrhage he had come to the conclusion that the only satisfactory way of dealing with this was to take the patient back to the theatre, give him a further anæsthetic and tie the bleeding point. He had entirely given up all the medical means of dealing with reactionary hæmorrhage, as these were often uncertain and merely prolonged the anxiety.

On the question of secondary hæmorrhage, he made no distinction between hæmorrhage on the fifth day, and what was known as true secondary hæmorrhage, occurring about the eighth day. A former President of Laryngology, Mr. Musgrave Woodman, had taught him many years ago to use pure carbolic acid in the treatment of secondary hæmorrhage, and this he invariably used as a local application to the tonsil bed, without disturbing any blood clot, on the initial signs of secondary hæmorrhage occurring any time after twenty-four hours from the time of the operation. Carbolic acid was a local anæsthetic and a local antiseptic, and in his experience its use had always led to cessation of this complication.

Mr. G. A. Fraser said that whilst no one would allow a patient to die from hæmorrhage, depression of the respiratory centre as a result of over-sedation from further anæsthesia and post-operative medication might well escape notice.

Owing to hæmorrhage, cyanosis might be partially or totally absent, and in that case anoxæmia would only show itself by restlessness. If the cause of this was not recognized and further sedation was given, it would not only quieten the child but kill it.

If a child had to go back to the theatre, anæsthesia should therefore be light, and further post-operative sedation avoided. He considered that most deaths were not directly due to hæmorrhage, but to anoxæmia which escaped notice owing to the absence of obvious cyanosis in a partially exsanguinated child.

Dr. J. Middleton Price said that a few words from an anæsthetist might not be out of place, as on return to theatre this was mainly an anæsthetist's problem.

On the use of depressant drugs in children, he said they must remember that ether could be just as depressant as thiopentone or pethidine. In particular, it was completely wrong to condemn "modern" anæsthesia because of allegedly slow recovery. He normally used rectal thiopentone followed by nitrous oxide with small doses of pethidine and trilene, and a relaxant, and the majority of children were wide awake on leaving the theatre, although not unduly restless. Mr. Fraser had said that no patient should ever die from hæmorrhage, and all anæsthetists should insist that the blood volume was restored before return to theatre. The main cause of death was from inhalation of blood and vomit and it was essential both to empty the stomach before the anæsthetic was commenced and to follow with tracheobronchial toilet (Morton, A. J., and Wylie, W. B., 1951, *Anæsthesia*, **6**, 190).

The use of thiopentone and a relaxant had been advised, but, if used, the patient should be placed in a *foot*-down position to prevent regurgitant vomit. It was also an essential to use an orotracheal tube with a cuff or pack. As in any difficult case, the anæsthetist was of far greater importance than the choice of anæsthetic.

Miss Winifred Hall said that in her opinion, except in very rare cases, tonsillar hæmorrhage was preventable, and could be prevented in the theatre by taking time to ensure complete hæmostasis before the patient was sent back to the ward, and the surgeon should be prepared to spend as much time as was necessary on this.

Other essentials were an experienced anæsthetist, adequate premedication, a quiet induction and maintenance of full anæsthesia until the operation was complete, and all bleeding completely stopped. It was also most advisable that during the recovery period the patient should be in the care of experienced staff, both medical and surgical.

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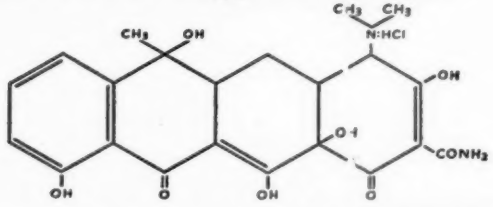

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[*April* 21, 1954]

DISCUSSION ON TONSILS AND ADENOIDS

Dr. Oliver Plowright: The problem of enlarged tonsils and adenoids is essentially one for the general practitioner. The trouble is mainly one of childhood; we know that lymphoid tissue tends to regress after the age of 12–15 years. After that age there is no problem of treatment: "When in doubt, take them out." They have served their purpose and can be dispensed with if there is reasonable evidence of their doing any harm. Further, the operation at that age, though more uncomfortable in its early convalescence, does not carry with it even the modest dangers that are present with the operation in the younger age-groups.

It is generally accepted that the tonsils and adenoids form a ring of lymphoid tissue in the pharynx which is protective against infection inhaled through the nose and mouth. Having made this introduction I want to put in a strong plea for the separation in our minds of adenoids from tonsils. The phrase "Ts and As" has become so time-honoured that I find it difficult to get many people, parents, nurses and even doctors, to dissociate the one from the other, though I think that when it comes to treatment it is of the utmost importance that this dissociation should be made. The indications for the removal of the adenoids are straightforward and the decision easy to make. Apart from the very rare case of gross congenital enlargement of the adenoid pad the problem is unlikely to arise before the age of 2½ or 3 years and should certainly have been settled by the age of 6 or 7.

The indications are: (1) Gross nasal obstruction producing constant mouth-breathing and snoring when asleep, even when there is no coryza present. This is an important point as so often the child is produced when he has a bad cold and no fair judgment can be made. In this connexion one should be very much alive to the possibility of allergic rhinitis causing nasal obstruction. (2) Recurrent attacks of otitis media with or without otorrhœa. The presence of deafness, again when no coryza is present, is an added impetus to removal under this heading. The objection may be raised that removal of adenoids only may necessitate a second operation later for tonsillectomy. We must accept this risk unless there is strong evidence for removal of the tonsils at the same time.

The problem of how best to deal with diseased tonsils is more difficult. In the last three decades the operation for tonsillectomy has become extremely common and still is so. On what grounds do we send so many of our child patients to have their tonsils out? What are the indications? If we can accept the fact that the tonsils act as a barrier to inspired infection, then we must expect them to grow larger under repeated infections and I believe that upper respiratory infections in young children are very much more common now that they go to nursery schools at 2½ or 3 years of age. On the question of chronic infection of the tonsils I have been able to discover no large-scale investigation of the bacteriology of the tonsils and the pathologists disagree as to what are the criteria of infection in the tonsil, even after its removal. Probably, we all have our own ideas of what a chronically infected tonsil looks like but it is extremely difficult to prove the infection and its chronicity. I doubt if there are any *general* indications for tonsillectomy as opposed to the *local* indications. The theory of focal sepsis is debatable. There is conflicting opinion on the value of tonsillectomy in nephritis and rheumatic fever but, as far as I know, there is no evidence that the operation is of any value in either disease, particularly in these days of antibiotics and sulphonamides. The *history* should help us in coming to a decision. Certainly, frequent attacks of tonsillitis (say three in two years) or the history of a quinsy should persuade one that the tonsils need to come out, but we must be careful to distinguish true tonsillitis from ordinary sore throats.

A history of frequent colds is no indication for tonsillectomy, though removal of obstructive adenoids may well reduce the stubborn post-nasal drip that so often follows colds in children and will certainly reduce the danger of otitis media during a cold. I consider that repeated upper respiratory infection is largely the result of overcrowding in home and school life, though there may be an inherited lack of resistance to such infection as well. Removal of the tonsils is likely to hinder rather than help the child's fight against such infections. It is better to remove the child from its environment rather than the tonsils from the child.

One of the difficulties we doctors are up against is that in assessing the effects on the child both of the affected tonsils and of their removal, we are considerably dependent on the opinion of the parents. Quite unjustifiably, the operation for removal of the tonsils has achieved a tremendous reputation among parents who will badger us until, in desperation, we are forced to agree that "perhaps they had better come out after all". After this build-up it would be surprising if the same parents did not see quite a startling improvement in their children after the operation, though very often they will confess that it was two years afterwards before it appeared. Even in the present state of our knowledge it should be possible to lay down a few definite indications for the removal of tonsils in children. (1) Frequent attacks of tonsillitis with persistently apparent infection in the tonsils between attacks and persistently enlarged and tender lymph nodes. (2) After two and, possibly, after one quinsy. (3) When the tonsils are so large as to cause obstruction of respiration—probably a very rare occurrence, though in relation to this point I think that chronic infection of the nasal accessory sinuses may sometimes be kept up by grossly obstructive adenoids and tonsils. (4) Diphtheria carriers, where other treatment has failed.

Having laid down these absolute indications I must admit that I occasionally see quite startling improvement in the growth, appetite and general well-being of children whose tonsils have been removed for less obvious indications, and I only wish I knew why. Once the decision to operate has been made—and I consider that it should be made by the general practitioner in conjunction with the throat surgeon with the additional advice of the pædiatrician in particularly difficult cases—it is essential that it be done under general anæsthesia by careful dissection and by a competent expert. Tonsillar remnants left after guillotining or imperfect dissection can be a great source of trouble, though in fairness to the operator they must be distinguished from regeneration of lymphoid tissue in the tonsillar fossæ. It is sometimes quite satisfactory for the operation to be done in the child's home, provided it is a suitable one. This avoids a good deal of psychological trauma and reduces the risk of cross-infection as well as the queue for hospital beds. I usually give a shot of procaine penicillin prophylactically while the child is under the anæsthetic, though there may be some criticism of this practice from the point of view of subsequent penicillin resistance. At least it may combat the transient bacteriæmia that has been proved to follow removal of infected tonsils.

The dangers of tonsillectomy are inconsiderable but nevertheless they do exist and it is therefore important to decide that the operation is really necessary. (1) Official figures show an average of 85 deaths per annum under the age of 15, directly due to tonsillectomy. (2) Hæmorrhage following the operation does occur and not so very infrequently, though I am sure that it is largely an avoidable risk if adequate time and care are spent over the operation. (3) Deaths under general anæsthesia cannot be entirely ignored. (4) Nervous disturbances, such as night terrors, enuresis, &c., constitute a reason for considering the decision very carefully. (5) Poliomyelitis; the figures for the incidence of bulbar paralysis following tonsillectomy during an epidemic of anterior poliomyelitis are still conflicting.

Finally there is the question of research in general practice on this vexed question of enlarged tonsils and whether and when they should be removed. (1) No satisfactory bacteriological study of tonsillar infection has been carried out. For example, the removal of tonsils harbouring hæmolytic streptococci might provide better results than removing the tonsils in a wholesale fashion. Does the infection disappear after the operation? (2) A comparative study might be made of the results of a course of treatment with one of

the newer antibiotics as compared with tonsillectomy for chronic infection of the tonsils. (3) Selected practitioners from different parts of the country and with different types of practice might pool their observations on the incidence of sore throats and the growth in height and weight of children in the twelve months following tonsillectomy as compared with the twelve months immediately prior to the operation.

Dr. Wilfrid Sheldon: *Symptomatology of Adenoids.*—It is important to realize that the adenoids have a symptomatology which can often be distinguished from symptoms attributable to the tonsils, and cases undoubtedly arise in which the adenoids should be removed but the tonsils may well be left alone. Although one still occasionally encounters the surgeon who is not prepared to make this distinction, but insists on the "all or nothing" law, such an unenlightened attitude is fast disappearing.

Of the symptoms mainly due to the adenoids, I would put snoring first. Snoring is due to vibration of the uvula and soft palate and requires mouth breathing for its production. It is therefore associated with nasal obstruction, of which adenoid enlargement, although not the only cause, is certainly the most common. Recurrent infection of the middle ear, and repeated episodes of deafness, are much more often associated with adenoid infection than with tonsil infection, and I suspect that the same holds true for infection of the accessory nasal sinuses, which we have come to recognize as a fairly common ailment in children beyond the toddler age. I agree with Dr. Plowright that congenital hypertrophy of the adenoid pad is uncommonly met with, but is an occasional cause of interference with an infant's sucking, for which a closed mouth is necessary, and when such a condition is present, removal of the hypertrophied adenoids, even in young infants, is clearly indicated. I should say that interference with sucking from this cause is not so rare as congenital atresia of the posterior choanæ.

Another symptom suggestive of adenoid infection is vomiting in the early morning before breakfast, particularly if the vomit contains large quantities of mucus. Presumably this comes about from the child swallowing a good deal of mucopus from the nasopharynx during the night, the stomach rejecting this material as soon as the child begins to move about. It is, of course, necessary to exclude other possible causes of morning vomiting such as a raised intracranial pressure or severe renal disease.

Before leaving the subject of the adenoids and nasal obstruction, something must be said about allergic rhinitis, for which I am sure many children undergo a needless removal of their tonsils and adenoids. Allergic rhinitis is not only common, but is just as powerful a producer of nasal obstruction as is adenoid enlargement, but the history is different. The allergic child so often starts the day with a bout of sneezing that enquiry for this symptom is always worth while. On the other hand deafness and middle-ear infection is not a likely complication. Examination of the nasal mucosa in allergic rhinitis shows it to be much swollen and pale in colour, with the airway between the septum and inferior turbinate much reduced, and still further blocked by the secretion of a highly glistening watery mucus. There is often a story that the child blows his nose vigorously but is quite unable to clear his air passages. Often too, these children lose much schooling, because at school the dust of the classroom excites the nasal mucosa, and by the time they return home, they present all the symptoms of "yet another cold". Enquiry shows that such "colds" are not infectious, and do not spread round the other members of the child's home, but the anxious parent complains bitterly that as soon as the child goes back to school he gets another "cold". Their misinterpretation of the symptoms should be fully explained to them. This is not the place to expand further into the causation and treatment of allergic rhinitis; let it suffice to say that removal of the tonsils and adenoids in a child whose nasal obstruction is due to allergic rhinitis is bound to be disappointing, based as it is on an incorrect diagnosis.

Function of the tonsils.—This is often described as a trap to catch infections entering by the oral route. To take the analogy further, a trap is an instrument that has to be set, and is later sprung. It is then reset to be ready for the next victim. An acute attack of tonsillitis

represents the springing of the trap, but if after a few days the tonsils return to a healthy state and the cervical glands, which have been enlarged in the acute phase, return to insignificant size, then we can say that the trap has been reset. A good trap can be reset many times, and in my opinion removal of the trap—or tonsils—should not be advised simply and solely because the child has had several attacks of tonsillitis, from each of which the throat has recovered perfectly. Under such circumstances it might be wiser to examine the rest of the household to discover whether some other member is the source of recurrent infection.

It is a different matter if it can be shown that the trap is broken and cannot be reset. The best evidence of this is when the glands at the angle of the jaw remain persistently enlarged and firm, although not necessarily or usually tender. This is an indication that the tonsils are unhealthy (assuming of course that no other cause such as dental, mouth, or skin infection is present), and are no longer able to serve their purpose. Less reliance is to be placed on the appearance of the tonsils, for when diseased they may be either enlarged, or much scarred and contracted; but such appearances as dilated vessels coursing over the anterior faucial pillars, or granular fauces and uvula, are also evidence of chronic infection.

A decision to remove the tonsils ought never to be made during the phase of acute tonsillitis; time must be allowed to ascertain whether the tonsils are capable of returning to a healthy state, and the cervical glands able to return to insignificant size.

On the question of tuberculous cervical glands, I do not believe that tuberculous infection reaches these glands via the blood stream. There is ample evidence that primary tuberculous infection, wherever it is located, tends to spread along the lymphatics to the regional lymph glands, and if the tonsils of a child with tuberculous cervical glands are removed and submitted to histological examination, foci of tuberculosis can always be found in them. It is certainly my practice when dealing with a child with tuberculous glands in the neck, to recommend tonsillectomy, and to have the tonsils examined histologically, though whether the tonsils should be dealt with before or after surgical treatment of the glands must depend on the state of disease in the glands, and, of course, not all such glands require surgical treatment. Nevertheless the tonsils should be removed, in the hope of preventing further glands from becoming involved.

Reverting to septic infection of the tonsils, I am not at all sure that the theory of focal sepsis is by any means dead. When recurrent tonsillitis is followed by repetition of acute hæmaturic nephritis, I should prefer the tonsils out of the way, and if there is evidence of chronic tonsillar sepsis in company with such collagen diseases as rheumatoid arthritis, or dermatomyositis, it is usually wise to eradicate the focus of infection. There is no doubt also that such symptoms as a bad appetite, unpleasant breath, and failure to thrive may at times be dependent upon chronic infection of the tonsils, and the child continues to ail until the source of infection has been removed. Although such cases call for careful judgment and a diligent exclusion of all other possible causes, if the right case is selected there can be no doubt about the benefit that may follow tonsillectomy.

Parents often ask what is the best age for removing the tonsils and adenoids, and I think the answer is that when there is evidence that these structures are persistently unhealthy, and are exerting an adverse influence on the general health, or are causing such local troubles as enlargement of the cervical glands, recurrent middle-ear infection or deafness, then that is the correct age for operation, no matter what the chronological age may be.

Finally, though I have no doubt that in the hands of an expert a perfect removal of the tonsils can be performed with the guillotine, I believe that this is an instrument for experts only, and that otherwise removal by dissection is to be preferred. It is difficult to find an excuse for an incomplete removal of the tonsils, and if this does occur, then the operation has failed. I have always felt differently about removal of the adenoids, which is a blind performance, and one where excessive vigour can do harm. A later recrudescence of adenoid symptoms after these structures have been removed is therefore likely enough now and again, but with regard to the tonsils only complete extirpation will give a perfect result with no recurrence of local inflammation or infection.

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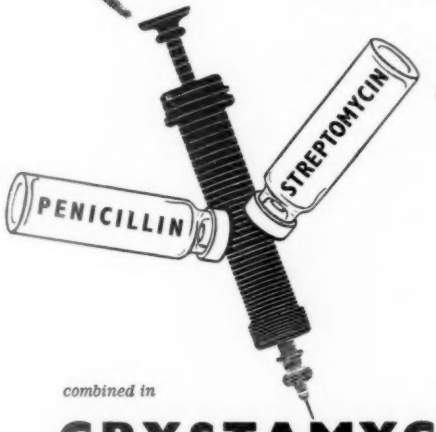

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[*May* 19, 1954]

DISCUSSION: PHYSIOLOGICAL AND PATHOLOGICAL ASPECTS OF LOCOMOTION IN MAN AND ANIMALS

Professor C. W. Ottaway (Dept. of Veterinary Anatomy, The University, Bristol):

Physiological Aspects in Animals

A discussion on locomotion in man and animals can afford to be introduced from a general biological viewpoint. Before specialization to one or more species—and the variety of species of vocational concern to the veterinary surgeon provides most interesting examples of locomotory capabilities—all have a common interest in the Animal Kingdom as a pre-medical discipline. Comparative anatomical thought may also be of value to the problem of muscle rehabilitation in man. Mackenzie (1945) has suggested that when considering re-education of injured muscles it is necessary to review all possible functions and that on evolutionary grounds it may be profitable to practise a mode of action differing from that usually executed by the normal muscle. A further value to a "four-legged" introduction is that it may early focus attention on the advantages and disadvantages of having an extra pair of props or propellers: they certainly affect balance and are of help in standing for long periods provided the necessary support structures are present. On the other hand how often may an extra pair of weight-bearing limbs mask symptoms of lameness in one of the other pair?

These general thoughts need not lead to consideration of complex nervous mechanisms or structural detail, but they could and should lend emphasis to an important principle that whatever the particular study it is really necessary to regard the whole body as a single functional locomotory unit, as advocated by Sir James Gray. There is, of course, a non-party feeling among the locomotory tissues, as exemplified by the variable action of complex or two- or three-jointed muscles. Sir Frederick Smith introduced this type of thought to the veterinary profession in the last decade of the nineteenth century, and his early lead at a time when modern methods for analysis of muscle action were unknown deserves commendation; Smith's approach was observational not experimental.

It will be freely admitted that the arrangement of structures in any limb of any species is in keeping with an established pattern of locomotory behaviour, whether it be for the purpose of movement or support; a pattern which has slowly evolved and has been influenced also by environment. For this and other reasons it may be argued that the pattern so established is not very efficient, but when the multi-purpose of locomotory structures is considered it may be agreed that evolution has not made so bad a job. After all, though it is true that the mole could run better if his legs were straighter it must be remembered that his main objective is to retain the ability to burrow. The further question may be asked: if in the course of evolution a species or group of species has acquired a particular habit in a particular region, for example method of movement of hip or shoulder, will analysis of that particular arrangement help in assessment of the true purpose of locomotory tissues? Or, as a subsidiary question, in the establishment of that particular arrangement have neighbouring parts been neglected in such a way as to produce weak anatomical spots predisposing to injury?

As a method of learning it is customary to analyse the working of a simple locomotory unit before proceeding to the study of more complex units, when such factors as secondary movers—John Hunter's

original term—and fixation muscles must be considered. But even straightforward analysis, certainly in the dissection room, will soon raise the query of how often a joint or part will move to the limit allowed for by its anatomy; for example the vertebral column viewed as an isolated anatomical structure will certainly allow more movement than is commonly practised in locomotion. When working together with other areas the summation of movement of a region will perhaps utilize but part of its apparent potential for the simple reason that its range is controlled by surrounding tissues. On the other hand limit of use may be determined by habit alone, as may be instanced in regard to the educated habit: there is nothing abnormal about the movement of an acrobat or of a high-stepping hackney pony. A further point on the possible as opposed to the practised is consideration of the culminating point of an action such as the human leg-kick or the flick action of a horse in removing an offending fly from the elbow. Both of these movements are possible and practised but are not of the sustained variety, and the limb cannot be retained in that position. On the general question of the possible as opposed to the practised, is abuse of the usual, within the limit of the possible, sufficiently regarded as a predisposing factor to injury?

Of the many structural changes in animals associated with the evolutionary triumph of elevating the body off the ground, few had more pronounced effect on locomotion than re-orientation of the shoulder and pelvic girdles, for, not until shoulder and elbow were applied to lateral thorax and pelvis firmly united to the vertebral column was fast four-footed running possible. The arrangement of the shoulder in the domestic species, indeed in most fast-moving mammals, presents a most interesting array from the locomotory point of view.

The shoulder-joint.—With laterally applied weight-bearing limb in the absence of a clavicle, the shoulder-joint moves in the longitudinal plane but more extensive is movement of the entire shoulder region on the thorax during both the non-weight-bearing stage of protraction and the weight-bearing stage of retraction. The need during different stages of the cycle is to fix the shoulder-joint, to move the shoulder region and to accommodate to impact on the ground. Outstanding in effecting these actions are muscles such as the supra- and infra-spinatus, deltoid, teres major, latissimus dorsi and the ventral serrate. The sum total is that the fore-limb, in the shape of the shoulder, moves on the chest in a manner not dissimilar from that of a car chassis moving on springs, up and down while accommodating to the possible uneven nature of the ground, as well as forward and backward, continuing the simile, comparable with movement of the car wheels. Another term may be introduced into consideration of this type of shoulder movement, "scapular glide"—forward and backward movement of the scapula on the chest wall—which may be viewed quite independently of the angulation of joints. It undoubtedly occurs, and is an aid to progression if for no other reason than it lengthens the stride. There are, therefore, many biological reasons why the veterinarian should pay regard to the shoulder as a potential seat of lameness.

The hip-joint is an area of great anatomical fascination. The comparative anatomist will regard the angulation of femoral head and neck to femoral shaft, the depth of acetabular cavity, the size and shape of the teres ligament, the presence of accessory intra-articular ligaments, the set of femoral trochanters, the arrangement of the close musculature particularly the gluteals, as the most important anatomical features for the consideration of the clinician. In regard to anatomical features predisposing to dislocation a survey of the domestic species does not reveal any outstanding factor. It is, however, true that the only domestic species possessing an accessory ligament of the hip is the horse, and in this animal dislocation is very rare. The function of the teres ligament is not clear: at one time it was regarded as a structure assisting in preventing dislocation, now more is heard of its function of providing, in early life, a pathway for a vessel nourishing the proximal femoral epiphysis. Has the ligament a dual function? In some animals it is short and certainly could assist in retaining the femoral head, but in others it is relatively long and could seemingly have no such effect. The age factor must also be considered, and indeed the finding of a vessel in the young animal of some species.

The stifle or knee may be regarded in many ways as the key joint of the body. For the veterinarian it has an additional feature of interest in that it is never straight and has therefore to contend at all times with the flexing force of gravity. The horse gets over the problem of the bent stifle at rest by locking the patella. The contour of femoral trochlear lips and the arrangement of patellar ligaments is such that following contraction of the quadriceps muscle the patella glides upwards, outwards, and then inwards to halt on the articular boss situated at the limit of the articular surface of the trochlea, in which position the patella is locked in the plane of flexion and extension. This mechanism has been described by Shuttleworth (1944). Seemingly the way in which the lock is released is for the patella to move in the reverse direction from that described for locking, i.e. first outward, at which point it may glide downwards and inwards. If this is true the biceps femoris and tensor fascia lata could be the responsible muscles. This activity is a pronounced feature of the resting hind-limb of the horse. At times the lock, or excess of the lock, occurs when the animal is unable to release, the creature standing immobile in field or stable. Manipulation relieves, when the animal usually promptly runs off at great speed and with great ease, but it is liable to recur. The horse is able to rest a single hind-limb with a minimum of muscular effort, for, once the stifle is locked the largely tendinous

nature of the fibularis (peroneus) tertius and plantaris aid synchronized locking of the tarsal joint, and the tendinous interosseous medius or suspensory ligament is largely responsible for the state of the fetlock. The suspensory ligament, the modified interosseous muscle of the sole remaining weight-bearing digit to be compared with the fleshy interosseous of man or dog, is a most interesting structure. Functionally the need of this muscle is to support the fetlock; this it can perform better in ligamentous form, and Nature has accommodated. The generalization may be advanced that animals which spend a deal of their life in the standing position, such as the horse, have a relatively higher proportion of tendinous tissue in the limbs than those such as the dog which assume the recumbent position whenever possible. A high percentage of tendon fibre may, however, have repercussions in cases of paralysis, for recovery of tendon tissue is reputed to be much slower than muscle.

A feature associated with the difference between the objective and subjective approach to diagnosis is the possible accommodatory action of muscles taking the place of injured units in such a way as to mask symptoms. Experiments on animals and observations of an experimental or clinical nature have indicated that animals can get along fairly well without the use of even a major unit. Provided the injury is not gross or at certain critical points, immediate accommodation is possible from other structures suitably placed for the purpose. There may be pain, but no apparent physical effect or change of gait, thus the veterinary clinician is at a marked disadvantage to his medical confrère. It should, however, be stated that although a unit may be capable of performing more than one type of action there is but one action for which it is primarily designed.

In cases of peripheral nerve injuries in animals do we pay sufficient regard to the site and nature of the lesion? For example, clinical cases of radial paralysis in the weight-bearing limb exhibit symptoms of a dropped elbow and knuckling over of the metacarpo-phalangeal joint. As these symptoms indicate interference with the triceps musculature as well as with the extensors of the manus, such cases are usually attributed to nerve injury fairly high in the limb, usually in the axilla. In the course of experiments on the dog directed toward advancing knowledge of the functional anatomy of the limb the main tendons of the triceps were sectioned immediately before insertion on to the olecranon process. The result was that the limb was held in a position typical of radial paralysis. Yet in another experiment when the radial nerve was sectioned peripheral to the origin of branches to the triceps, central to the origin of branches to the extensors, extension of the foot was certainly affected but the posture and movement exhibited were in no way typical of radial paralysis. This would seem to indicate that injury of the branches to the triceps alone is sufficient to cause a radial paralysis, and not that the lesion need involve the main trunk.

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Dr. Eric Wynn Jones:

Pathological Aspects of Locomotion in Animals

Some general problems of disease of the locomotor apparatus as they occur in domestic animals are discussed. Infections are excluded.

Treatment of congenital and hereditary defects with the exception of the domestic pet presents no problem. Diagnosis and controlled breeding are, however, of real importance, especially as a result of the development of artificial insemination and the consequent narrowing of the genetic base of the livestock concerned. Instigation of adequate control measures may often be difficult owing to the breeders' unwillingness to admit the presence of the condition.

The occurrence of certain traumatic conditions emphasizes the importance of the anatomical weak spot especially when there is often a direct relationship between the comparative incidence and comparative anatomy of the condition, especially functional anatomy. The most common dislocation in animals is that of the hip. The domestic animal bears more of its weight upon the anterior limb, while the function of the posterior limb is that of propulsion. This dislocation in the larger animal usually results from sudden excessive weight-bearing such as that associated with slipping or struggling to rise. In the small animal it is usually due to direct trauma. Dislocation of the hip is commonly observed in the ox, dog and cat but very rarely in the horse. The latter animal has an accessory ligament originating from the prepubic tendon and which is inserted on to the head of the femur. Abduction of this joint is consequently limited.

In the case of fractures direct trauma is usually incriminated in the small animals and indirect in the large. In the latter the offending movement is often well within the limitations of the range of movement of that joint or limb but is one which is not commonly used and to which muscle co-ordination is not adequately educated. The occurrence of disease associated with an abnormal

pattern of locomotion is further exemplified by tendinitis of the flexors of the digit in the horse. A bruised foot will cause an altered pattern of locomotion, weight-bearing upon that hoof will be uneven, and the limb may be abducted or adducted during flight. As a result of this, tendinitis will often result. Similarly, tendinitis may occur when acute lameness in one foot results in excessive weight-bearing on the opposite.

Diagnosis.—The greatest problems arise in the larger domestic animal. Control, localization of pain, and palpation are all frequently limited by size and muscle bulk. These factors also limit the extent to which X-ray diagnosis may be used. Recent research suggests that a kilovoltage of at least 220 will be needed to obtain radiographs of the trunk of the cow and horse. At present, for instance, the possibility of repairing a fractured humerus or femur in a larger animal can only be adequately assessed by exploration at operation. With these difficulties in mind, the importance of recognizing patterns of locomotion characteristic of disease in any one part becomes obvious. Dislocation of the hip for instance is manifested by flexion, adduction and outward rotation. During progression the limb is incompletely extended, the affected limb often being carried anterior to the normal one. Arthritis of the tarso-metatarsal joint is manifested by inward rotation, incomplete flexion and dragging of the toe. The need to consider at least the entire limb or even the complete body as a functional locomotor unit becomes increasingly obvious when secondary muscle atrophy or even secondary lameness develop. Atrophy of the supra- and infra-spinatus is a common complication of disease of the foot, while atrophy of the gluteal muscles is observed in chronic arthritis of the tarso-metatarsal joint.

In treatment, whether it be operative, rest or controlled movement, many basic problems exist especially in the large animal. During operations the procurement of satisfactory anæsthesia along with control of muscle spasm and adequate relaxation has been difficult. The ability to use positive-pressure respiration and consequently, relaxants, in the large animal has materially assisted this. Limitation or control of the post-operative course is difficult. This has been especially troublesome when repairing fractures in the ox by the use of intramedullary nails, for it is often essential that the pin used shall be the only means of support. In the small animal such problems do not present the same difficulties. On the other hand the advent of skeletal fixation has resulted in an ever-increasing tendency to obtain anatomical perfection in alignment, rather than, and sometimes at the expense of, a good functional result. To illustrate some of the points mentioned films of clinical cases were shown.

In this short essay, an attempt has been made to indicate some of the problems of locomotor disease in animals, especially the large domestic animal. The importance of correlating present knowledge and future research with comparative functional anatomy is stressed.

Mr. Norman Capener (Exeter):

Pathological Aspects of Locomotion in Man

It is recorded that Isaiah took exception to certain haughty daughters of Zion who "walk with stretched forth necks and wanton eyes, walking and mincing as they go, and making a tinkling with their feet". Such and other peculiarities of gait are of recurring interest to mankind throughout the ages and the more pathological aspects of locomotion provide the material for the greater part of that field of medicine which is orthopædics.

In the evolution of the erect posture a major development has been the elevation which has occurred in the lower spine and hip-joints. Man's final state should be regarded rather as the *extended posture*, for it is very different from the erect posture assumed by terrestrial avians and any other bipeds or quadrupeds who may occasionally assume a biped posture. In radiographic studies which I made of a dog in its normal posture and when standing on its hind-legs, extension of the hips is not very great in the last-mentioned position but such as it is, it causes little, if any, alteration to the lumbosacral angle. This, however, is very different in the case of newborn infants, who, when *in utero* have both hips and spines fully flexed, yet can immediately, by extending the hips (though this is incomplete), be made to produce the lumbar curve which is characteristic of all normal humans in standing.

Hip extension in infants is not complete until several years after birth, and this largely explains the normal lordotic or pot-bellied appearance of babies when first they walk. Partial return to the flexed state of the hips is one of the signs of degeneration in mankind and the flexed lumbar posture is one of man's vulnerable positions in which the vertebral arrangement bears a striking resemblance to the human fœtal and to the quadruped curves. This is of significance in the modern stress which results in lesions of the intervertebral joints and considerable locomotor disability. In human evolution there has been a relative lengthening of the hind-limbs which, with the extended lumbar spine and hip-joints, was associated with a centre of gravity placed within the pelvis. The art of walking and standing involves the easy and economical control of the centre of gravity.

The scientific study of human locomotion goes back almost 100 years, notably to work in Germany by Fischer and Braune. Inman and his associates in California have described the determinants of normal gait which cause the centre of gravity to follow a smooth pathway in walking. Professor Ottaway has described the rotary movement in lower animals and the evolution of straighter pathways. That humans take a rotary action is obvious to all who will observe their own movements in relation to surroundings when walking down a long, narrow corridor, particularly if there is a mirror at the end. Saunders, Inman and Eberhart have shown how the movements of the pelvis, hip, knee and ankle-joints convert what would otherwise be a jerky gait in which the centre of gravity would pass through a series of arcs of high amplitude, into a smooth sinusoidal curve of low amplitude which causes the centre of gravity to take a low spiral movement through space. The determinants, which are those of pelvic rotation, pelvic tilt, knee flexion, ankle flexion and obliquity of the femoral shaft, lead to economy of energy. Conversely, any circumstance increasing the amplitude of movement is expensive. The body is able to compensate for stiffness in one of the hip, knee or ankle joints by increased activity in the remaining components, so as to maintain an almost identical pathway for the centre of gravity; in the case of the knee this is less so than in the other joints, for though the knee contributes little to the normal propulsion of the body through space, it does contribute greatly to the smoothness of the pathway of the centre of gravity and therefore to the reduction of energy requirement. Stiffness of two joints in a limb makes very heavy demands upon the cardiovascular system in this regard. It is clear that to maintain a smooth walking or running gait involves a complex series of movements in the joints of the lower extremities, and that the co-ordination of the neuromuscular mechanisms is highly complex. In the interpretation of these complexities Professor Arthur Steindler has played a leading part, particularly in his exposition of the work of the German physiologist von Baeyer. While we appreciate Sherrington's work on reciprocal innervation and the problems of muscular synergic relaxation, we, in orthopædics, are perhaps inclined to over-emphasize the function of muscles as prime movers, synergists, antagonists, &c. We tend to think too much of the prime action of muscles in which, being fixed centrally, they operate peripherally in what von Baeyer calls an open kinetic chain. Of equal importance and of particular significance in relation to conditions of labouring is the circumstance described by him as the closed kinetic chain, in which the peripheral resistance to muscular action was greater than the central resistance. Von Baeyer demonstrated this principle in a simple form by showing that a kinetic chain is closed from foot to hand through the intermediary of the earth and a laden wheelbarrow. Common enough as such a circumstance is in labouring men, the idea of the closed kinetic chain must be of great significance in animal locomotion, where such a chain is the constant situation in quadruped progression. In man it can produce many types of muscular paradox; as, for example, in such a situation as pushing against a resistance, here the triceps muscle can give flexion of the shoulder-joint, and in pulling against resistance the biceps can extend it. Steindler has given examples of many of these paradoxes in the lower extremity, and I will mention three of these in relation to the soleus muscle. The first, when the foot is flat on the ground with the knee bent the soleus muscle has the power of extending the knee; when only the toes are touching the ground, the heel off, then by further plantar flexor action by the soleus it has the effect of flexing the knee-joint; in the same position when the knee is extended the soleus may cause adduction of the hip and elevation of the pelvis. In man the function of the hand provides a striking parallel with conditions seen in quadrupeds. The grip of surgical forceps between the thumb and index finger illustrates a typical closed kinetic chain and demonstrates that extension of the terminal interphalangeal joint may be importantly affected by the action of the flexor sublimis muscle attached to the middle phalanx. Pathologically, as Sir Harry Platt has emphasized, the idea of the closed kinetic chain is of significance in the development of trick movements in paralytic lesions and in the development of vicious postures and deformities in arthritis. In the disturbances of two-joint muscles there are peculiar problems in relation to the closed kinetic chain.

In orthopædic work we are very much aware of the tremendous forces which are set up in the body by muscular action associated with leverage and the factors of acceleration and deceleration. Of special interest are the researches of another group of American workers as recorded in particular by Elftman. This concerns the torque or turning moments exerted by muscles upon joints. We realize that the number of foot-pounds involved in muscular action is very considerable and is variable under conditions of angle of pull, length of lever and the length tension state of muscle fibre. Elftman has shown that flexion and extension of a joint like the hip in walking or running are not just simply flexion and extension so far as the forces on the hip are concerned. There is a most complex variability of torque with muscles alternating between extension and flexion throughout the simple movement in one direction or another.

Another problem with which we as orthopædic surgeons are concerned is that of bones as levers and supports, and it is in the hip-joint that we find much to concern us. Here studies in the past have too often been related to the femur as a static device. We appreciate the significance of its shape in relation to the forces of compression, tension, shear and torsion. What has been neglected, however, is the distribution of stresses within the neck during the complex movements which it undertakes not only as a weight-bearing structure, but in its dynamic capacity as a propeller shaft, in moving the body

forward and in restraining its movement, and as a means of conveying propulsive power to external objects.

In considering human joint function it is important that we should not only bear in mind the complexities of motive power such as I have already outlined, and the mechanical principles of leverage which bones provide, we must also recognize that joints have bearing surfaces which must be protected in the same manner as in engineering bearings by proper lubrication. It is in this last problem that much remains to be done by research before we can satisfactorily achieve the surgical ideal of reconstructing joints which have worn out as the result of osteoarthritis. Our problems therefore are mechanical, biological, pathological, psychological and economic. Overshadowing everything in the biological plane is the integrity of the vascular supply of moving parts, bony structure and of the muscles which control. Bone is both an elastic and a vital plastic material, and we have to admit that at present no satisfactory solution has been found for the conjunction of inert material with a vital mechanical system. Steindler has picturesquely referred to the complexities of muscular activity in human gait as being not unlike a symphonic score, in which muscles enter into the pattern at certain moments and leave it at others. The older writings on human gait were abstruse, physical and mathematical treatises, difficult for the practising clinician to understand. The work of such people as Steindler, Inman and other modern American investigators has done a great service in presenting the material in more simple terms, and it is clear that we have much to learn in our clinical practice from the data now being made available.

(The paper was illustrated by diagrams taken from the writings of the authors mentioned, and also by examples from clinical practice.)

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Correction.—*Proceedings*, Vol. **47**, p. 747, September 1954. *Section of Comparative Medicine.*

The Function of Antibiotics in Animal Nutrition.—S. K. KON. Line 6.—"12 mg./ton food" *should read* "12 g./ton food".

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JOINT MEETING No. 5

Section of Comparative Medicine with Section of Epidemiology and Preventive Medicine

Chairman—Professor T. J. BOSWORTH, M.A., B.Sc., M.R.C.V.S.
(President of the Section of Comparative Medicine)

[*February* 17, 1954]

DISCUSSION: GASTRO-ENTERITIS: THE ÆTIOLOGICAL IMPORTANCE OF VIRUSES AND *BACTERIUM COLI*

Professor R. E. Glover (Dept. of Veterinary Pathology, Liverpool): *Neonatal Diseases of the Calf*

Scouring in calves is a general term which probably embraces a number of different entities, some of which are specific and some non-specific. There has been a tendency of recent years to introduce the designation "pneumo-enteritis" to cover conditions in which diarrhœa is accompanied by an involvement of the respiratory tract: the use of this term is possibly unfortunate and it may have led to confusion in the consideration of the different causes of losses in the young calf. The diseases of the calf are probably due to at least three main causes. First there is the nutritional scouring which has been admirably reviewed by Blaxter and Wood (1953), who take the view that many of the cases are due to a form of indigestion, particularly liable to occur with pail feeding. There is no evidence of actual inflammation unless a bacterial infection supervenes. The *Bacterium coli-Salmonella* type of infection which Professor Lovell and his colleagues have thoroughly investigated is usually associated with involvement of the intestinal mucosa so that a catarrhal enteritis of a varying intensity is set up. In this disease pneumonia may supervene as a secondary complication. There may be, however, a not inconsiderable group in which the respiratory tract is primarily infected, but in which diarrhœa occurs in the terminal phases. These are prone to be classed as pneumo-enteritis, but in fact there is no evidence of involvement of the intestinal mucous membrane. The situation has been summarized by Udall (1946), who says: "More often the pneumonia is primary in the sense that the initial and dominant symptoms are respiratory, or the respiratory symptoms may be immediately preceded by diarrhœa. Thus typical pneumonia epidemics may be ushered in with or without diarrhœa."

Withers (1952, 1953) gives tables showing over-all death-rates in calves. Like many investigators he tends to differentiate pneumonias in which *Bact. coli* or other organisms occur from those in which no bacteria are found, regarding the former as manifestations of calf scours, but it is quite possible that in the first group the bacteria are secondary to some other agent.

Attention has already been drawn to a form of pneumonia in calves occurring in the north-west parts of the country where there are significant losses due to a pantropic virus with particular pneumotropic affinities, the disease often being complicated and accentuated by secondary bacterial invaders of which the most common causal organism is *C. pyogenes* (Jennings and Glover, 1952). Barr *et al.* (1951) showed that most of the cases of this disease occur in the late winter and early spring, with an age incidence varying from one to two days to about two months after birth. There is a seasonal peak which is probably associated with marked changes in temperature, and this seasonal incidence fits in with the statement of Withers: "Climate appears to be the chief extrinsic factor influencing calf mortality, the most serious losses from *Bact. coli* infection occurring from January to April."

The disease in calves may run an acute course, but at some stage there is usually coughing and a mucopurulent nasal discharge. It is just as likely to attack well-managed as poor farms, and occurs in calves receiving colostrum and in those which are pail-fed. In both the natural disease and the condition we have set up experimentally there is an acute turbinitis and varying degrees of inflammatory changes in the lungs together with generalized lymph node enlargement. The agent appears to be a filtrable virus. One of the most constant features is a febrile reaction commencing about the fifth day at which stage the virus is present in the blood stream. Constipation in the early stages is followed by diarrhœa of varying intensity. The degree of involvement of the lungs is accentuated by chilling the calves or by administering with the virus a secondary organism. In the uncomplicated virus infection, however, the lesions in the lungs may be relatively slight, but they are always accompanied by an enlargement of various lymphatic glands.

The constant involvement of the turbinate region would seem to point to a primary infection of the upper respiratory tract, and the fact that the disease passes by contact, to an airborne infection. The scouring is in all probability a reflex action due to the effect of an agent which produces its most marked action on the respiratory tract, but is capable of invading other tissues. The more severe lesions are, in our opinion, a manifestation of bacterial invasion, the most important secondary organism being *C. pyogenes*. As is the case in other virus infections, there will be variations in different localities, and organisms predominant at one time will disappear at another.

The disease which we have been studying resembles quite closely that described by Lamont and Kerr (1939) except that they noted a rise in temperature in their experimental calves starting at the twenty-fourth hour and continuing for ten days. The condition investigated by Baker (1942) is

particularly interesting because his virus is clearly pneumotropic, and the calf disease picture much resembles that described by us. His agent, however, was readily transmissible to mice, whereas all attempts to adapt our virus to small animals have so far been unsuccessful. Jarrett *et al.* (1953) believe that the disease in older calves described by them is due to a virus infection, and they set up changes in the respiratory tract by intratracheal inoculation. The natural disease was complicated, however, by parasitic infestation of the lungs. The salient pathological changes were mainly cuffing around the bronchi by hyperplasia of the lymphatic tissue, followed by compression collapse of the alveoli: these changes are quite different from those seen in the disease encountered by us.

Lamont and Kerr found Hæmophilus as secondary invaders in some calves and this organism has been isolated by Watt (1952) who set up pulmonary lesions by inoculating mouse lung infected from calf filtrates together with a culture of Hæmophilus. Thorp *et al.* (1942) also isolated Hæmophilus from the lungs and thought that the symptoms and lesions strongly suggested a combination of a virus and bacterial agent. An organism which is found in normal and in diseased lungs is *B. actinoides*: its significance in pneumonia is not clear as it is of low pathogenicity for calves (Blakemore, 1945), and for goats (Levi and Cotchin, 1950).

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Professor R. Lovell (Royal Veterinary College and Hospital, London): Bact. coli *and Calves*

During the last few years, a study of *Bacterium coli* infections in calves has been made by a group of workers at the National Institute for Research in Dairying, Shinfield, and the Royal Veterinary College. Calves are collected from farms around Reading and placed in special pens; no calf is accepted unless the result of a zinc-sulphate turbidity test shows that it has not suckled. Some calves are deprived of colostrum and these are probably responsible for the spontaneous occurrence of white scours. Post-mortem examinations are made and *Bact. coli* isolated from the bone-marrow, spleen, blood and other tissues. The common type isolated is the fæcal type 1; immune sera have been prepared against a selected number of strains and the identity of the somatic "O" and capsular "K" antigens determined. A number of serological types of *Bact. coli* have thereby been established and are recovered from time to time. Colostrum or one of its fractions is given to certain calves and at the beginning of a season the mortality in these calves is low; as the season progresses the mortality increases and eventually some of the calves receiving colostrum die. During the years 1950–51 and 1951–52 a total of 264 calves were received into the pens and of these 137 died and most of the strains of *Bact. coli* isolated from them were placed in serological groups.

Some strains have been examined by Dr. Ørskov of Copenhagen and one with the antigenic structure of 26 : B6 has been recovered from calves in this and other countries and also from babies. The common one from calves in this and other countries is one with the antigenic structure 78 : B; whilst another one 9: A has occurred during two seasons in spite of the vacancy of the calf pens for some months and their disinfection.

In an enclosed community subject to frequent immigration of fresh calves and under the conditions defined there is a constant occurrence of white scours. There is also a change in the bacterial flora and one serological type of *Bact. coli* is dominant for a time and this is replaced by another. The disease breaks out spontaneously if some of the calves are deprived of colostrum and no attempt to produce an infection has been made. It is therefore a hazardous procedure for a calf to be brought into a new environment shortly after birth and it is also dangerous for it to be deprived of colostrum. The equilibrium between calf and surroundings is disturbed violently and calf scours result.

Colostrum is essential for the survival and progress of the newborn calf and it has been shown that the factor concerned is that associated with the "immune lactoglobulins". Attempts were therefore made to determine whether any association exists between the specific antibody content of samples of colostrum and the serological types of *Bact. coli* which were prevalent in the calf pens.

The samples of colostrum fed to calves were therefore tested for their specific "K" agglutinins, and this enabled one to assess the protective value of samples of colostrum against a particular strain of *Bact. coli*. A very high proportion of samples of colostrum which had been given to those calves which survived, contained agglutinins against the prevalent strains of *Bact. coli* which killed contemporary calves. On the other hand, very few of the strains of *Bact. coli* which killed calves were agglutinated by the colostrum which had been given to the calves which died. The presence of

agglutinins against the capsular antigen of a particular strain of *Bact. coli* is correlated with protection against that strain, and there is an association between their presence in colostrum and the survival of calves receiving them. In contrast, the absence of specific agglutinins is associated with death and it appears therefore as if the protective value of colostrum lies in its content of antibodies against prevalent bacteria. The importance of colostrum and its specificity suggest that certain dairy practices may not be in the best interest of the calf. Calves may be deprived of colostrum, or the colostrum may not contain the specific antibodies. Prepartum milking may actually deprive the calf of colostrum. There is an undoubted hazard in removing the calf to a fresh environment after birth and it may be equally dangerous for the calf if the environment of the mother is changed just before it is born; the colostrum may contain antibodies against bacteria in the old environment but not against bacteria which attack the calf in the new environment.

Further work is proceeding and the principles established by our studies in the enclosed community are being confirmed in the field.

Dr. J. Smith (Regional Laboratory, City Hospital, Aberdeen): *The Association of Specific Types of* Escherichia coli *with Cases of Infantile Gastro-enteritis*

The idea that certain specific types of *Escherichia coli* have an ætiological relationship to infantile gastro-enteritis has been advanced by various workers. First attempts to define the relationship were made by Bahr and Thomsen (1912), by Adam (1923) and by Goldschmidt (1933) when they employed the fermentation characteristics of strains of *E. coli* to establish types. Bray (1945) was apparently the first to apply serological methods when he showed that in one particular outbreak an organism which he named *E. coli neapolitanum* could be isolated from most cases. With the publication by Kauffmann (1947) of his serological classification of the *E. coli* group of organisms the time was ripe for the reinvestigation of the whole problem. The organism isolated by Bray was found to belong to Kauffmann's *E. coli* group 0111B4, and further papers on the association of this organism with cases were published by Giles and Sangster (1948) and by Taylor *et al.* (1949). Another type 055B5 was identified in Aberdeen and four more, 026B6, 086, 0125, and 0126 were described by Taylor and Charter (1952), another was found by Smith (1953), and more recently Cefalù and Brancato (1953) have found 025 to be the variety most frequently associated with cases in Italy. The three types 0111B4, 055B5 and 026B6 can be further subdivided by certain fermentation reactions and more particularly by the identification of their "H" antigens. Thus, "H" antigens 2 and 12 have been identified in certain strains of 0111B4, and 2, 6, 7 and 21 with 055B5 and H11 with 026B6. These subdivisions are particularly useful in epidemiological studies and have been fully utilized by Wright *et al.* (1953) in their studies on cross infection.

In Aberdeen in the autumn of 1946 an infectious form of infantile gastro-enteritis not due to organisms of the Salmonella or Shigella groups became prevalent in various children's wards and nurseries. Deaths in children under 1 year of age due to enteritis rose in the city from 9 per 1,000 births in 1946 to 22 in 1947 and fell again to 5 in 1948 and the actual morbidity, though the disease is not notifiable, appeared to follow the same trend. Afterwards the decline in both incidence and severity of the disease continued and for the past three years no deaths have occurred. Infantile gastro-enteritis varies so markedly in its manifestations that it is often difficult, on a clinical basis, to distinguish between the infectious and non-infectious forms, and, furthermore, many mild cases of diarrhœa and vomiting occur in which it is often not possible to distinguish between enteral and parenteral causes. On the other hand as research has continued more specific types of *E. coli* have been found to be associated with cases occurring in groups.

In 1947 specific types were associated with 240 cases of whom 104 died, while in the years 1948 and 1949, 62 and 78 cases with 17 and 1 deaths respectively were similarly associated. In the succeeding years up to the end of 1953, 36, 50, 22 and 20 cases with no deaths were found to harbour specific types. Thus in a total of 508 cases, of whom 122 died, specific types were isolated. In a certain number of severe cases and in a larger number of mild and doubtful cases none of the recognized specific types was isolated. Experience during the past seven years has shown that the mild and doubtful cases from which no specific types of *E. coli* or any member of the Salmonella or Shigella groups have been isolated, seldom, if ever, occur in epidemic form, and seldom, if ever, give rise to cross infection.

In 1947, 233 strains of type 0111B4 were isolated, 30 in 1948, and 8, 2, 1, 5, in the succeeding years up to 1952, and none in 1953, a total of 279 strains of which 255 were obtained from clinical cases and 24 from excreter contacts. Subdivided on the basis of the sucrose fermentation reaction which, when positive, indicates an H2 and when negative an H12 antigen, 242 strains were sucrose positive and 37 sucrose negative. Furthermore the sucrose negative sub-type with the H12 antigen disappeared first and was last isolated on 3.11.50 while the H2 sub-type continued to be isolated until 12.8.52. The death-rate in cases associated with the 0111B4 type was markedly greater than in those associated with any other variety, for out of a total of 255 clinical cases 105 died.

The number of strains (358) of the 055B5 type isolated from 216 clinical cases and 142 excreters was greater than the number of 0111B4 strains. In the years 1947 to 1951, 38, 67, 109, 65 and 74 were recovered, and so far as could be determined all these had the H6 antigen. In 1952 one H6, two H7

and one H21, and in 1953 another H21 strain was isolated. The deaths in clinical cases associated with 055B5H6 totalled 19 out of 216. There were no deaths in the small groups of H7 and H21 infections. The original H6 sub-type was last isolated on 21.8.52, some eighteen months ago. The 026B6 type was first looked for in 1950 and the total isolations since that time have only been 34, and all strains, with one exception, have been isolated from clinical cases. Strains of this type can be divided into 3 sub-types as described by Ørskov (1951). Twelve sub-type 1 strains which have no "H" antigen were isolated in 1950 and 1951, none in 1952 and 14 in 1953. Two strains of sub-type 2 were isolated in 1952 and 6 in 1953. The third sub-type which is an anaerogenic form has only been recovered once, and that in 1953. Though many cases associated with this organism were quite severely ill there were no deaths. Types 086, 0125, and 0126 have been searched for since 1950 also but only 1 strain of 0126 has been encountered locally though this type has been prevalent in an outbreak which occurred last year in an Edinburgh hospital. Type 0119 was first encountered in May 1952, when the strain of *E. coli* obtained from a severe case could not be identified by the sera then in use. An antiserum was prepared for this particular organism and later in the year further sporadic cases were encountered, and then a small outbreak of 6 cases occurred in a hospital ward; from the same source 10 more strains were obtained from immediate contacts without symptoms of the disease. A number of severe cases of infantile gastro-enteritis have occurred in which no specific type of *E. coli* could be isolated. In 15 such cases, 10 strains from each primary plating have been retained and an "OB" agglutinating serum prepared from one strain from each case. Almost invariably it has been found that all 10 strains obtained from one case have belonged to the same serological type and cross-agglutination tests of strains from different cases have failed to show any serological relationship. What the significance of these findings is at the moment, it is difficult to determine.

During the past seven years, therefore, the epidemiology of an infectious form of infantile gastro-enteritis has coincided with the distribution of the specific types of *E. coli*. The disappearance of the original 0111B4 and 055B5 types has been associated with marked reductions in morbidity and mortality. The outbreaks of the disease in wards and nurseries, often following upon the transference of infants from wards or nurseries known to harbour infected cases, the isolation of a particular serological type from the infants in the primary outbreaks, from the transferred infants, and from the cases in the secondary outbreaks, were common occurrences during earlier epidemic years but these incidents have now ceased. The epidemiological and bacteriological findings must indicate therefore an ætiological relationship. Many problems such as the infrequent production of antibodies following upon an attack of the disease, the essential difference between infectious and non-infectious forms of *E. coli*, and the mode of action of the specific organisms in the intestine require much further investigation.

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Dr. R. L. Worrall: The search for a general causal agent in diarrhœa and vomiting of infants calls for a chemically known, antigenic substance satisfying the following conditions:

(1) It must be obtainable from non-pathogenic bacteria, including *E. coli*. (2) On administration to animals, it must cause pyrexia and diarrhœa. It must be (3) filtrable; (4) resistant to heat; (5) susceptible to pH changes; and (6) subject to biological assay.

A pyrogen satisfies these conditions, in so far as it is a filtrable, antigenic polysaccharide, obtainable from *E. coli*, *B. proteus*, *Staphylococcus aureus* and other bacteria, causing pyrexia when administered parenterally to animals, in a dose as small as 1 microgram per kilogram of body weight. Diarrhœa and death occur with mounting dosage. A pyrogen can be assayed by its leucocytic effect on rabbits. A pyrogen is resistant to boiling water and even to autoclaving at neutral pH, while on the acid side of neutrality it is destroyed by boiling.

At a recent joint meeting of the Society of Public Analysts and the Pharmaceutical Society, I suggested that pyrogens may constitute the general chemical cause of infantile diarrhœa and vomiting. For the investigation of this possibility, I have suggested to Mr. T. D. Whittet, of University College Hospital, the oral administration of a pyrogen to very young animals and also to adults of the same species. A contrast in response between very young and adult animals would strengthen the view that pyrogens constitute the general chemical cause of infantile diarrhœa and vomiting. Acidification of water used to clean utensils could also be tried, as a means of dealing with outbreaks in hospital

Section of Ophthalmology

President—HUMPHREY NEAME, F.R.C.S.

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Uveitis in Childhood

By A. G. CROSS, M.D., F.R.C.S.

UVEITIS is one of the commonest conditions met with in ophthalmic practice. It is responsible for much loss of time in industry and in business, and it results in a considerable degree of blindness. It is caused by many different factors, some definite and some speculative, and among all the cases which are seen a large proportion are of undiagnosed ætiology.

Uveitis is less common in children than in adults and it seems possible to establish the ætiology in a larger proportion of juvenile than of adult cases, or at least to classify them into clearly defined groups. In the young, a more pure strain of the disease would appear to be produced, and so it may be worth while studying the types found in children in order to help solve the overwhelming basic problem of the ætiology of uveitis. This communication is based on a series of patients in whom the onset of uveitis was before the age of 16 years.

Uveitis is a suitable name for this clinical entity because, in the large proportion of cases, the condition is not confined either to the iris, the ciliary body, or to the choroid. Most parts of the uveal tract are affected to some extent in every case. In anterior uveitis the iris and ciliary body are predominantly attacked, while it is the choroid which is mostly inflamed in cases of posterior uveitis.

In cases of pan-uveitis there is an equal reaction throughout the uveal tract. The terms iritis, iridocyclitis, and choroiditis are now obsolete.

ANTERIOR UVEITIS

Causes and Groups: Syphilis—Interstitial keratitis. Acute specific fevers. Tuberculosis. Sarcoidosis. Still's disease. Brucellosis. Vogt-Koyanagi syndrome.

Syphilis of the congenital type causing interstitial keratitis has always been one of the most usual causes of anterior uveitis in children. It is becoming far less common as a result of the introduction of antibiotic drugs. The efficient treatment of syphilis in pregnant women with penicillin has reduced greatly the incidence of interstitial keratitis in the children, while the cases which do occur as a result of the use of cortisone are not nearly so likely to suffer permanent visual disability as in the past. Indeed, it is possible that this condition may become a rarity within our generation.

Acute specific fevers may occasionally cause uveitis whether they be due to bacterial or virus agents. Most of these conditions seem to have a septicæmic phase before the disease becomes more localized, and transient uveitis has been seen in children both in meningococcal meningitis and in rubella; it has been described in others of the exanthemata. It is possible that the condition occurs not infrequently in mild form, and proceeds to spontaneous and complete cure.

Tuberculosis is undoubtedly a cause of anterior uveitis in children. An infection of the iris and ciliary body by the tubercle bacillus occurs rarely, but when it happens it seems that it progresses to cause serious damage of the eyeball and often its loss. I have not had the opportunity to treat such a case with streptomycin, PAS, or isoniazid, but a few cases seen previously to the introduction of these drugs, deteriorated steadily until the eyeball had to be removed. The affection of the eyeball by a sensitivity to the products of toxins produced by the tubercle bacillus is a different problem. This is an acknowledged cause of uveitis in adults and in children throughout the world, though the incidence in children has never been clearly defined. The incidence in adults varies greatly in the statistics of different writers, possibly due to the difficulties of diagnosis, which tends to be made on inadequate evidence and by a process of exclusion. The points which are helpful in diagnosing tuberculous anterior uveitis of the sensitivity type are a history of present or past tuberculosis either in the patient or in his family, or of other contact with tuberculous patients; the presence of a positive Mantoux reaction (though it must be realized that this only indicates a skin sensitivity and not a uveal sensitivity to tuberculin); and the clinical attributes of large "mutton fat" K.P., iris nodules and an associated sclerokeratitis. To this can be added the therapeutic test which suggests that four to six months under a sanatorium regime of rest, graduated exercise and adequate nourishment, should cure any lesion of a tuberculous type. No serological test is available, similar to the Wassermann reaction in syphilis, to indicate the presence of active tuberculosis. A series of tests with the Middlebrook Dubos test which Dr. N. Ashton and Dr. R. W. Riddell have carried out in patients from the Eye Sanatorium at Swanley, has been quite inconclusive both in adults and in children.

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It is interesting to note that phlyctenular keratoconjunctivitis, usually regarded as a tuberculosis sensitivity reaction, used to be a common condition but that any associated uveitis was rare.

Sarcoidosis is a cause of uveitis in children though this condition is rare in the young. The ocular inflammation may be an isolated, or almost an isolated, manifestation of the condition, or it may be associated with a generalized state of sarcoidosis affecting many tissues of the body. The clinical manifestations are so characteristic as to allow a provisional diagnosis of the condition to be made, and it is possible that it is a more common cause of uveitis than is generally appreciated. The predominant features are the large profuse K.P. which have a ground-glass appearance, in contrast to the more yellow appearance of the K.P. which is characteristic of tuberculosis. The Mantoux test is usually negative, not always a significant point in children where this is a common finding. BCG inoculation will, however, usually produce a positive Mantoux reaction in children, in the absence of sarcoidosis. Other manifestations of the condition are sometimes found, especially in the lymph glands of the mediastinum. When affected lymph glands exist near the skin surface, they may be excised so that histological examination can confirm the diagnosis. The albumin-globulin ratio of the plasma proteins is often disturbed, showing an elevation of the globulin fraction, and the erythrocyte sedimentation rate may be raised. Nodules in the iris may occur, but these are not always present. The treatment of generalised sarcoidosis by systemic cortisone and by ACTH may be prolonged and require a large dosage, but the treatment of anterior uveitis due to sarcoidosis by local application of cortisone drops gives very satisfactory results. It is important to remember that uveitis occurring in a child may be an indication that sarcoidosis is present in the body, and that it may spread to other tissues.

Still's disease.—This condition in which rheumatoid arthritis accompanies anterior uveitis in children is a well-recognized syndrome. The uveitis is chronic in type, and is not associated with large or profuse K.P. It is, however, associated with a plastic type of exudate, with band degeneration of the cornea, and with complicated cataract. The uveitis may precede the arthritis or it may develop after the joint changes are manifest. It may be uniocular or binocular and the inflammation may settle down at any stage of its development. A very characterististic complication of the condition is the cataract which tends to come on steadily at a fairly early stage in the disease. It appears that both this and the band degeneration of the cornea must be regarded as due to a change in the constitution of the aqueous humour, as a result of the effects of inflammation upon the ciliary body, with resulting changes in the nutrition of the lens and cornea. The surgical treatment of these cataract cases is a matter of extreme difficulty because frequently the active uveitis persists for a long period, and there is a tendency to shrinking of the eyeball. There is a considerable risk that attempts to remove the lens while the active uveitis persists may result in phthisis bulbi. It is worthy of emphasis that it seems that cases occur of "Still's disease without arthritis". Certainly, cases of uveitis occur in children which show the characteristic plastic uveitis, band degeneration of the cornea, and complicated cataract, and in which arthritic changes never develop. Some of these cases are regarded as of tuberculous ætiology, but often they show none of the characteristics of that condition which have previously been enumerated. It is certain that these cases tend to have a uniformly bad prognosis. Local cortisone therapy and a sanatorium regime appear to do little to help, while the whole battery of antibiotics may be employed without avail. It may be that, with ACTH and cortisone becoming more easily available, these preparations may be used systemically. This is certainly justified as a sight-saving treatment since it would appear that the causative agent is transient, even if sometimes of long duration. Cataract extraction in these children is fraught with the same dangers as in those with arthritis, and even with a "cortisone umbrella", success is questionable.

Brucellosis may be a cause of uveitis in children. The diagnosis can be determined clearly from skin tests, and from brucella agglutinin and complement-fixation tests. Usually a chronic uveitis is associated with nummular keratitis.

Vogt-Koyanagi syndrome.—This syndrome which, when complete, comprises bilateral uveitis, poliosis, vitiligo, alopecia, and dysacousis has occurred in my experience in two children. The cause of this condition is uncertain but it is thought to indicate an inflammation of the meninges, and possibly of the hypothalamic region of the brain. It has been suggested that this inflammation is either due to a specific virus or as the result of tuberculosis, but it might equally well be due to a sensitivity factor which is also responsible for the uveitis.

Posterior Uveitis

Causes and Groups: Toxoplasmosis. Syphilis. Tuberculosis. Exudative choroiditis.

This condition can occur in children, but like anterior uveitis it is not common. In some of the patients, anterior uveitis may also be present, but in these cases the posterior uveal tract is predominantly affected.

Toxoplasmosis.—This is, possibly, the commonest cause of posterior uveitis in childhood. It is the result of a maternal infection with the toxoplasma parasite and was fully considered by the Section of Ophthalmology on February 11, 1954 (*Proceedings*, **47**, 481). Evidence is accumulating in the United States of America that toxoplasmosis may cause not only posterior uveitis but also

perivasculitis retinæ and anterior uveitis. The various tests for toxoplasmosis are therefore essential in the routine investigation of all cases of uveitis in children.

Syphilitic posterior uveitis.—This has been a frequent cause of uveitis in children, usually causing the well-known picture of disseminated choroidoretinitis. This condition, like interstitial keratitis, is often the result of congenital syphilis and it has become very much less common on account of the more efficient treatment of syphilis in expectant mothers.

Tuberculous posterior uveitis.—This condition like tuberculous anterior uveitis is not always easy to diagnose. The typical tuberculoma presents a characterististic appearance, but this is not commonly seen. The multiple tuberculous nodules associated with miliary tuberculosis and with tuberculous meningitis are well known in these days when streptomycin and allied drugs cause life to be prolonged in these cases. More doubtful in origin are those patches of solitary choroiditis, believed by some authorities to be tuberculous in origin. These patches are often quiescent when seen and the diagnosis of the cause has to rest upon the same indeterminate factors which have to be considered when considering the diagnosis of tuberculous anterior uveitis.

Exudative posterior uveitis of solitary type is seen in children fairly frequently. The appearance of a fluffy exudate in the fundus, with vitreous opacities, and sometimes with K.P. is characteristic. Some of these cases may be due to toxoplasmosis and some may be tuberculous in origin, but the ætiology in the majority is obscure. Some of the children are prone to hay fever and asthma. The condition tends to run a course and to settle, leaving choroidoretinal scars, and this is often helped by the use of cortisone or of ACTH and though there is some tendency to recurrence the condition does not usually cause serious visual disturbance unless the macula or its immediate area is affected.

Pan-uveitis

Causes: Sympathetic ophthalmitis. Non-specific pan-uveitis.

This type of inflammation affects the whole uveal tract in like amount and frequently it causes severe visual disturbance. It often tends to be bilateral.

Sympathetic ophthalmitis is the most common example of this type of ocular inflammation and little need be said about it here. It is not common but it occurs sufficiently frequently, and more often in children, to keep it constantly in our minds in casualty departments and in the wards, when perforating injuries have occurred. The true malignant type of sympathetic ophthalmitis remains a therapeutic problem. In spite of the use of cortisone and ACTH it still seems that there is little that can be done to halt this condition once it has developed. In almost all cases the result is total and complete loss of vision, both in the exciting and sympathizing eye.

Non-specific pan-uveitis.—These children sometimes appear in the neurological departments of hospitals, because though there is often a complaint of defective vision, the main finding on examination of the eye is a blurring of the optic disc which may suggest plero-cephalic œdema. Careful examination of the eye always shows fine K.P. with flare and with cells in the aqueous humour. The whole uveal tract is inflamed and patches of choroidal scarring may appear. It seems that the inflammatory condition spreads to the optic nerve, and these cases may suffer rapid and often complete loss of vision in both eyes, the end-result being an optic atrophy of secondary type. If they are recognized and it is essential that all cases of optic neuritis should be examined for the presence of uveitis, these cases can be controlled and the sight can be preserved by the adrenocortical hormones.

Ætiology.

Having discussed the main types of uveitis which are found in children, it is possible to consider the extent to which they help us in deciding the ætiology of the whole condition. It is agreed that some cases of uveitis are due to protozoal or bacterial infection, that some are due to viruses, and that, in all probability, the remainder are due to sensitivity reactions. Toxoplasmosis uveitis is an example of a protozoal infection, while tuberculous uveitis, brucellosis uveitis, and syphilitic uveitis are of bacterial nature.

The sensitivity theory seems to satisfy the cases due to tuberculosis where no bacteria are present within the eye, and sarcoidosis, which, though there are many theories for its cause, may be regarded as a state of generalized sensitivity to some antigen. Even Still's disease might fall into this category, and it is possible that interstitial keratitis is essentially a sensitivity reaction of the cornea and uveal tissues to the presence of the *Treponema pallidum*. The cases of uveitis in which other manifestations appear, like the Vogt-Koyanagi syndrome, might also be due to a sensitivity reaction of tissues outside the eyeball, as well as to tissues of the uveal tract.

The virus theory would appear to fit more satisfactorily our knowledge of sympathetic ophthalmitis, and Still's disease could, of course, have a virus origin. The Vogt-Koyanagi syndrome also could be due to the spreading effects of a virus infection.

The problem remains unsolved. Continuous efforts must be made to isolate a virus from cases of uveitis, and, at the same time, the immunologists should seek to demonstrate in animals a variety of sensitivity reactions similar to those which appear in the condition of uveitis in humans. The work which is being carried out in the United States on the sensitivity reaction of the many strains of

streptococcus appears to be of great importance. The immunity reactions of children appear, in general, to be less complex than those of adults and it may be that, in this field, the sensitivity reactions of uveitis can be solved.

The President said that Mr. Cross had referred to tuberculosis forming massive exudates. He presumed the lesion was of a similar character to the so-called tuberculoma sometimes seen in the eyes of human beings and also of animals. The appearance had been reported in the eye of a cat and he was able to examine one such case in which there was a large single tuberculoma of the choroid.

Mr. O. Gayer Morgan said that one sometimes saw youngish people of 16 or so, but also older persons, complaining of misty vision. They had a vitreous haze and in the fundus there was evidence of old choroido-retinitis and an active focus, very often a part of the old scar or in its neighbourhood. Sometimes one would find in a sector—curiously enough an area of the fundus which seemed to involve one retinal vessel—several of these scars and an active small new focus which had produced the vitreous haze. Could these be due to toxoplasmosis? In other words did toxoplasmosis have later periods of activity which one could see clinically? He did not think it did. But these cases of choroidoretinitis in a certain sector of the fundus were quite common and, if they were choroidal, it was curious that they should always be associated with one particular sector, which corresponded with the arrangement of the retinal vessels. Did Mr. Cross think that these cases were due to a local sensitivity of retinal tissue so that if the patients got run down or had some other illness they would develop a new active spot of choroido-retinitis?

Mr. F. G. Hibbert asked whether Mr. Cross felt that the degree of retinal reaction—retinal œdema—was really due to irritation. Were some of these cases primarily neuro-retinitis?

Mr. E. F. King asked whether Mr. Cross found it easy to differentiate cases of uveitis into granulomatous and non-granulomatous varieties as suggested by Professor Alan Woods.

Mr. R. W. Stephenson said that Mr. Cross had mentioned Still's disease and anterior uveitis. He would suggest that this might be in the nature of a total reaction. He recalled the case of a girl who had Still's disease and under cortisone the activity of the disease was reduced and cataract extraction was carried through smoothly. The pupillary area remained fairly clear. Unfortunately the vitreous was so full of deposit that there was no possibility of any good visual result.

Mr. W. K. Smiley said that he had been interested in Still's disease for about five years and during that time he had examined over 100 children with juvenile rheumatoid arthritis. Of this number about 5 or 6% showed ocular changes. This proportion was not nearly as high as was suggested in reports from Denmark where it was stated that 20% of children with Still's disease showed an anterior uveitis, very often with a band opacity. Of the few he had discovered in the last few years two were now in Blind Homes. One of them was interesting because the eye changes developed two-and-a-half years before any signs were shown in the joints and it was only by a strict follow-up of the case that one was able to prove that it was a case of Still's disease. He tried to remove the cataract from one eye in this case under local cortisone protection. He got rid of the cataract quite well but he found that the vitreous was so opaque that the child's vision was not better and indeed the eye did not seem able to withstand the surgery. Eventually it became soft and shrunken. The other eye also had a complicated cataract, but one would rather hesitate to operate on it except that one felt the child had nothing to lose.

Another case with a cataract did better, and again there was fairly rapid disappearance of the cataract by needling, but many vitreous opacities remained and vision was 6/36. The other eye was blind. This patient also had bilateral band opacity and one felt that a lamellar graft might be necessary. He thought that he might be able to get this patient out of the Blind School where he was at the moment. With Still's disease one could have an irreversible condition of post-cyclitic vitreous opacities which defeated all one's efforts even if the cataract was removed. One of his cases was a girl who had gross corneal band opacities and whose photograph he had shown at the meeting. Looking at her one would never imagine that she could see to read, but fortunately she had not got cataract and the band itself seemed to be a relatively insignificant factor in visual impairment. The vision was 6/9 in one eye and 6/18 in the other, and she could read and do quite fine needlework. He had two other children on treatment with cortisone which seemed, temporarily at least, to cure the uveitis, but, of course, the condition might well recur when treatment stopped.

Mr. F. J. Curtis asked whether Mr. Cross had found malignant change to be at all common in posterior uveitis. He had in mind a boy of about 7 who started with posterior uveitis and developed a single lesion of the choroid which was subsequently found to contain malignant cells and the eye had to be removed. He wondered whether that often happened.

Mr. Cross, in replying on the discussion, said that the cases which Mr. Morgan had described fell into his classification of patients with the exudative type of posterior uveitis. The observation of the segmental distribution was one of interest and he was unable to provide any explanation for its cause.

In what he had described as non-specific pan-uveitis, K.P. was visible on the back of the cornea. There was also a flare in the anterior chamber. In his opinion the majority of these cases did not show excessive retinal œdema in the region of the disc. If such retinal œdema were present, it was unlikely that these cases would be confused with cases of plero-cephalic œdema.

On the question of the differentiation of granulomatous and non-granulomatous types of uveitis, he had purposely refrained from considering that problem, but in his opinion this conception had not greatly clarified the ætiology. It might be true that the uveitis of Still's disease was a pan-uveitis. He had always thought that the main inflammatory reaction was in the ciliary body and that the exudate from that region was responsible for the vitreous opacity. The case which Mr. Curtis had mentioned would be recalled by several members of the Moorfields' Staff. This child with retinoblastoma of one eye had attended with apparent posterior uveitis, and had later developed what appeared to be a hypopyon. The diagnosis of retinoblastoma had been confirmed on histological examination, after removal of the eye.

Section of Psychiatry

President—E. B. STRAUSS, M.A., D.M., F.R.C.P.

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The Concept of Man in Psychotherapy

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A WELL-KNOWN psychiatrist once said that Western Humanity had turned away from the priest to the doctor. Another psychiatrist complained that nowadays so many patients approached the medical man with problems which should really be put before the priest; but when one tried to send them to a priest they would not go. Actually, we find that patients repeatedly come to us with such problems as the meaning of their existence. It is by no means true, however, that we doctors attempt to carry philosophy over into medicine, though this is often said of us; it is the patients themselves who bring us philosophical problems—the problems of their own concept of life.

It may well be that the individual doctor, confronted with such problems, is somehow driven into a corner; but medicine, and psychiatry in particular, has thereby been compelled to review a new world of problems.

Even now, a doctor can make things easy for himself; just as before, he can escape from these new questions. For instance, he may escape into the sphere of psychology, proceeding as if the spiritual distress of a human being, striving for a meaning to his existence, were nothing but a psychological phenomenon and a pathological one at that.

Man lives in three dimensions: the somatic, the mental and the spiritual. Psychologism ignores this third dimension, the spiritual dimension—although this is the very one which *makes* a being human. It may often be that man's concern about a meaning in life, which should be worthy of life, is not in itself a sign of disease or of neurosis. The differential diagnosis between "achievement and symptom" —to use the antithesis of Oswald Schwartz—can only be made by someone who can see the spiritual. At any rate, the worry about the meaning of his life, the existence of this worry, this spiritual agony, may have very little connexion with a disease of the psyche.

Psychoanalysis has put forward its theory of the principle of pleasure; individual psychology has told us about the "Geltungsstreben". The principle of pleasure could be termed the will-to-pleasure; the Geltungsstreben, on the other hand, corresponds to the will-to-power. But where do we hear of that which most deeply inspires and pervades man; where is the innate, albeit often unconscious and sometimes even repressed, desire to give as much meaning as possible to one's life, to realize as many values as possible—what I would call the will-to-meaning?

Psychotherapy would turn this will-to-meaning—this most human phenomenon of all (since an animal certainly never worries about the meaning of its existence)—into a human frailty, a pathological phenomenon, a complex, or something of the kind. A therapist who ignores the spiritual, and is thus forced to ignore the will-to-meaning, is giving one of his most valuable assets away, for it is this very will-to-meaning that we should evoke, it is to this will that a psychotherapist should appeal. Again and again we have seen that, even under the most unfavourable conditions, both within and without, an appeal to continue life, to survive such situations, can only be made when such a survival appears to have a meaning. Above all, when a specific, personal mission is concerned; a meaning of existence, which can be realized by this one and only person; for we must not forget that every man is unique in the universe and we believe he exists but once in all time.

I remember my dilemma in a concentration camp when faced with a man and a woman who were close to suicide; both had told me the same thing—that they expected nothing more from life. In that moment the indicated therapy was to try to achieve a kind of Copernican switch by asking both my fellow-prisoners whether the question was really what we expected from life or, rather, was it not what life was expecting from us. I suggested that life was awaiting something from them. In fact, the woman was being awaited by her child abroad and the man by a series of books which he had begun to write and publish, but had not yet finished.

A goal can only be a goal of life, however, if it has a meaning. Now I am prepared for the argument that psychology and its medical application, psychotherapy, belong to the realm of science and are, therefore, not concerned with values; but I believe there is no such thing as psychotherapy unconcerned with values, only one that is blind to values. A psychotherapy which not only recognizes the spiritual, but actually starts *from* the spiritual, may be termed Logotherapy. In this connexion Logos is intended to signify " the spiritual " and beyond that " the meaning ". The Giessen psychiatrist, Richard Kraemer, once, so aptly, said with regard to logotherapy: Up to now the spirit was regarded " as the enemy of the soul " (he was referring to the famous book by Ludwig Klages); now the spirit has become fellow-fighter for the soul's health. Now we attack the disease with three armies: somatotherapy, psychotherapy and logotherapy.

It is, of course, not the aim of logotherapy to take the place of psychotherapy within the usual meaning of that term, but only to complement it, thus complementing the concept of man to form a picture of complete man, the completeness of whom includes essentially the spiritual dimension. In the first place such a therapy, which is directed towards the spiritual, will be indicated in cases in which a patient turns to a doctor because of spiritual distress and not actual disease. One can, of course, if one wants to, speak of neuroses even in such cases, neuroses within the widest sense of the term; the Utrecht psychiatrist Ruemke, has only recently said that neuroses are but syndromes. And if one speaks of neuroses in this very wide sense one may also call the despair over an unsuccessful striving for a meaning to life a neurosis, say an *existential* neurosis as opposed to the clinical neurosis. And just as, for example, sexual frustration may—at least according to psychoanalysis—lead to neuroses, it is also conceivable that a frustration of the will-to-meaning, may also be pathogenic, that is to say, may lead to a neurosis. I call this frustration existential frustration. The Head of the Psychotherapy Out-Patients' Department of the Neurological Policlinic in Vienna noted that 12% of the cases were existential neuroses. Ruth Volhard and D. Langen in their report on the Psychotherapy Out-Patients' Department of the Neuropsychiatric Clinic at Tubingen University (under Professor Kretschmer) found roughly the same percentage.

In these cases logotherapy is a specific therapy; in other cases it is a non-specific therapy; that is to say, there are cases in which the disease, in particular the neurosis, is psychogenic in the usual sense of the term, and yet the therapy can only be carried to its full success when concluded by logotherapy.

Thus we have shown when logotherapy is a specific therapy and when it can be effective though non-specific; but there are also cases in which it is no therapy at all, but something else, namely medical spiritual care. As such, it is to be used not only by the neurologist or the psychiatrist, but by every doctor, since, for example, the surgeon needs it just as much when faced with inoperable cases or with those that he must maim by removing a limb. Likewise the orthopædic surgeon is confronted with problems of medical spiritual care when he is dealing with cripples; finally, the dermatologist when dealing with disfigured patients, and the physician with incurables.

In all these cases there is, of course, more at stake than psychotherapy has hitherto been aiming at. Its aims were capacity to work and capacity to enjoy life; medical spiritual care is concerned with the capacity to suffer. Thus we are faced with an interesting problem; the question as to what fundamental possibilities there are at all of giving life a meaning, of realizing values. The answer is that life can be given a meaning by realizing what I have called creative values, or by achieving a task. But one can also give meaning to one's life by realizing experiential values, by experiencing the Beautiful, the Good, the True, or by experiencing one single human being in his uniqueness. And to experience one human being as unique, truly as Thou, means to love him. But even a man who finds himself in the most dire distress in which neither activity nor creativity can bring values to life, nor experience give meaning to it—even such a man can still give his life a meaning by the way in which he faces his fate, his distress, in which he takes his destined suffering upon himself as a burden to be borne; in this he has been given a last chance of realizing values.

Thus life has a meaning to the last breath. For the possibility of realizing values by the very attitude with which we face our destined suffering: this possibility is there to the very last moment. I call such values attitudinal values. The right kind of suffering—facing your fate boldly—is the highest achievement which has been granted to man. Thus, even where man must renounce the realization of creative and experiential values he can still achieve something. I should like to illustrate my point by the following case: A nurse in my department suffered from a tumour which was shown by laparotomy to be inoperable. In her despair the nurse asked me to visit her and our conversation revealed that the cause of her despair was not so much her illness in itself as her incapacity to work. She had loved her profession above everything and now she could no longer follow it,

hence her despair. What should I say? Her situation was really hopeless; nevertheless I tried to explain to her that to work eight hours or ten hours or any number of hours per day is no great thing, many people can do that; but to be as eager to work as she was, and so incapable of work, and yet not to despair—that would be an achievement few could attain. And then I asked her " Are you not really being unfair to all those thousands of sick people to whom you have dedicated your life as a nurse; are you not being unfair if you now act as if the life of a sick or incurable person, that is to say, of someone incapable of working, were without meaning?" I said: "If you despair in your situation, then you are behaving as if the meaning of our life consisted in being able to work so many hours a day; but in so doing you would take away from all sick and incurable people the right to live and the justification for their existence."

It goes without saying that the realization of attitudinal values, the achievement of meaning through suffering, can only take place when the suffering is unavoidable and unescapable.

It may well be asked if such an approach as I have described can still be said to belong to the sphere of medicine, and I can certainly be reproached with the fact that medicine thus extended can at least no longer be said to belong to the realm of pure natural science. For my part, I would then immediately admit that the methods of natural science are most certainly necessary, for instance, to amputate a leg; but I should just like to permit myself the question, how can pure natural science help us to prevent the patient from committing suicide, either after, or even before, the amputation? The great psychiatrist Dubois once said so rightly "Of course, one can manage without all that and still be a doctor, but one should realize that then the only thing that makes us different from a veterinary surgeon is the clientele".

Thus the fact remains that even where we, as doctors in the narrower sense of the word, must resign, we can still work as doctors in the wider sense by medical spiritual care, and I am sure that this work still belongs to the proper sphere of medical activity. Not for nothing did Emperor Francis Joseph II dedicate the great General Hospital in Vienna, which even to-day houses most of the university clinics: "Saluti et *solatio* ægrorum."

And how easy it is for a doctor to provide consolation. I should like to quote the case of a colleague, an old practitioner, who turned to me because he still could not get over the loss of his wife who had died two years earlier. His marriage had been very happy and he was very depressed. I asked him quite simply "Tell me what would have happened if you had died first and your wife had survived you?" "That would have been terrible", he said, "quite unthinkable; how my wife would have suffered." "Well, you see", I answered, "your wife has been spared that, and it was you who spared her, though, of course, you must now pay by surviving and mourning her." In that very moment his mourning had been given a meaning—the meaning of a sacrifice.

I have said earlier that man should not ask what he can expect from life, but should rather understand that life expects something from him. One might also formulate it like this: in the last resort man should not ask, what is the meaning of my life, but realize that he himself is the one on trial; life is putting its problems to him, and it is up to him to face the problems by shouldering his responsibility, thus answering *for* his life.

Life is a task, and religious man differs from the apparently irreligious one only by experiencing his existence not simply as a task but as a mission. This means that he also experiences the taskmaster, the origin of his mission. For thousands of years this authority has been called God.

I said before that logotherapy is no substitute for psychotherapy, but its complement; but least of all does medical spiritual care aspire to be a substitute for the proper care of souls; that is practised by the priest. Now, what is the relation between the medical and the priestly care of souls? What is the relation between psychotherapy and religious care? In my view the answer is simple: the goal of psychotherapy is to heal the soul, to make it healthy; the aim of religion is something essentially different—to save the soul. So much for the different aims of psychotherapy and religious care of souls. But if instead of asking what is being aimed at we try to see what is the result, the, so to speak, unintended side-effect, we will find that the side-effect of religious care of souls is an eminently psycho-hygienic one. This is due to the fact that religion provides man with a spiritual anchor and with a feeling of security, such as he can find nowhere else. But to our surprise, psychotherapy can produce an analogous unintended side-effect; for although the psychotherapist is not concerned with, must not even be concerned with, helping his patient to achieve a capacity for faith beyond restitution of his capacity to work, enjoy and suffer—in spite of this, in certain felicitous cases the patient regains his capacity for faith, although in the course of his psychotherapeutic treatment neither he nor his doctor had aimed at that.

For such a result can never be the aim of psychotherapy from the beginning, and a doctor will always have to beware of forcing his philosophy upon the patient. There must be no transference (or rather, counter-transference) of a personal philosophy, of a personal concept of values, to the patient. The logotherapist must be careful to see that the patient does not shift his responsibilities on to the doctor. Logotherapy is ultimately education to responsibility; and with this responsibility the patient must push forward independently towards the concrete meaning of his personal existence must choose it on his own. Thus we have spoken of the necessity and the possibility of psychotherapy,

particularly in the form of logotherapy, caring for the spiritual distress of contemporary man. Now that we have passed out of the sphere of the purely clinical into a meta-clinical domain, that of existential neurosis, we may process to the para-clinical realm of collective neurosis, the realm of a pathology of the "Zeitgeist", the spirit of our time, as one might call it.

Anxiety is usually called the disease of our time, and we speak of the age of anxiety; but Freyhan has pointed out that previous centuries probably suffered much more from anxiety and had much more reason for anxiety than ours. It is also very doubtful whether the relative incidence of anxiety neurosis has increased. Nor is it right to say that speed is the disease of our time, although one might gain that impression when faced with a phenomenon like "managers' disease". Of course, I am not referring to speed as the producer of increased numbers of accidents, though even here psychological elements—or rather spiritual factors—are dominant. As Joachim Bodamer recently has shown in Central Europe the car is to-day for the man in the street the highest criterion of a living standard, and the average man there frequently works himself to the bone just to buy a car for reasons of prestige; and then it may well happen that he falls a victim to the so-called "managers' disease". I know of cases in which people have, in this way, died of their car before they even owned it. Of course not everyone is satisfied with owning a *car*, and perhaps the most classical example of "managers' disease" I ever came across in my practice was that of a foreign industrialist who had only one wish, a wish that dominated his entire life: he was wealthy enough to afford a private plane, but cherished the ambition to own a jet instead. . . .

As far as one can speak about collective neurosis at all—in a purely para-clinical sense—the collective neurosis of our time is characterized by four symptoms, which I shall briefly describe.

First there is a planless, day-to-day attitude towards life. Contemporary man is used to living from one day to the next. He learnt it in the last World War and since then this attitude has, unfortunately, not been modified. While people used to live in this way because they were waiting for the end of the war and further planning, therefore, made no sense, the average man of to-day says: "Why should I act, why should I plan? Sooner or later the atom bomb will come and wipe everything out." And thus he slides into the attitude: "Après moi, la bombe atomique!" And just as any other anticipatory anxiety, this anxiety of anticipating atomic warfare is dangerous, since, like all fear, it tends to make that which it fears come true.

The second symptom is the fatalist attitude to life. This again has been learnt in the last World War. Man was pushed. He let himself drift. The day-to-day man considers planned action unnecessary; the fatalist considers it impossible. He feels himself to be the product or result of outer circumstances or inner conditions.

The third symptom is collective thinking. Man would like to submerge himself in the masses. Actually he is only drowned in the masses; he surrenders himself as a free and responsible being.

The fourth symptom is fanaticism. While the collectivist ignores his own personality, the fanatic ignores that of the other man, the man who thinks differently. The other man does not count, only his own opinion is valid. In reality his opinions are those of the group and those he does not really have; they have him.

Just as a normal conflict, a conflict of conscience, can become pathogenic by leading to an existential neurosis, so we can understand how as long as man is capable of a conflict of conscience he will be immune to fanaticism and to collective neurosis in general; conversely, a man who suffers from collective neurosis will overcome it to the degree to which he is re-enabled to hear the voice of his conscience and to suffer from it; existential neurosis will then cure the collective one! Some years ago I spoke on this subject at a congress where, among others, were colleagues who lived under a totalitarian regime. After the lecture they came to me and said: "We know this phenomenon very well: we call it 'functionary's disease'. A certain number of party functionaries are ultimately driven by the increasing burden of their conscience into a nervous breakdown and then they are cured of their political fanaticism."

Fanaticism crystallizes in the form of slogans, and these again produce a chain reaction; this psychological chain reaction is even more dangerous than the physical one, such as forms the basis of the atom bomb. For the latter could never be put into action if it had not been preceded by the psychological chain reactions of slogans.

Thus, if we speak of this pathology of the spirit of our time as of a mental epidemic, we might add that somatic epidemics are typical consequences of war, while mental epidemics are potential origins of war. In tests carried out by my collaborators with non-neurotic patients, only one was completely free of all the four symptoms of collective neurosis, whereas 50% of them showed at least three of the four symptoms.

Ultimately, all these four symptoms can be traced back to man's fear of responsibility and his escape from freedom. Yet responsibility and freedom compose the spiritual domain of man. Contemporary man, however, and this is characteristic, has become weary of the spiritual and this weariness is perhaps the essence of that nihilism which has so often been quoted and so rarely defined. This

would have to be counteracted by a collective psychotherapy. It is true that Freud once declared in conversation: "Humanity has always known that it possesses a spirit; it was my task to show that it has instincts as well". But I myself feel that humanity has certainly in the last years demonstrated *ad nauseam* that it has instincts or rather drives. And to-day it appears after all more important to remind man that he has a spirit, that he is a spiritual being. And psychotherapy itself should remember this fact, particularly in face of collective neurosis! And now we find ourselves immediately faced with the question of the concept of man in psychotherapy. Every form of psychotherapy has a concept of man, albeit not always consciously; but then it will be up to us to make it conscious. Or do we, who have learnt from Freud, really have to point out how dangerous the unconscious can become? We must explicate the unconscious, the implicit concept of man in psychotherapy, we must develop it just as one develops a negative, bringing it out of its latency towards clear manifestation. For a psychotherapist's concept of man, under certain circumstances, can be such that it reinforces the patient's neurosis, for it can itself be entirely nihilistic.

Three factors characterize human existence as such: man's spirituality, his freedom, his responsibility.

The spirituality of man is no epiphenomenon. It cannot be derived from and causally explained by something not spiritual; it is irreducible and indeducible. Spiritual life may very well be conditioned by something, without therefore being caused by it. Normal somatic functions are conditional to the unfolding of spiritual life, but they do not cause or produce it. Again I should like to illustrate this point by an advertisement from *The Times*, published some years ago: a witty gentleman inserted the following: "Unemployed. Brilliant mind offers its services completely free; the survival of the body must be provided for by adequate salary."

A normally functioning psychophysical organism is thus no more or less than the condition for the unfolding of the spiritual self.

Now freedom means freedom in face of three things: (1) the instincts; (2) inheritance; and (3) environment.

Certainly man has drives, but these drives do not have him. We have nothing against the drives, not even against man accepting them, but we hold that such an acceptance must presuppose that he also had the possibility of rejecting a drive, that there was thus freedom of decision. We have nothing against the acceptance of drives, but we are, above all, concerned with man's freedom in the face of them.

As for inheritance, the most serious research on heredity has shown how high is the degree of human freedom in the face of predisposition. In particular, research on twins has shown how different lives can be built up on the basis of identical predispositions. I should only like to remind you of the identical twins of Lange, where one partner became a cunning criminal, while his brother became an equally cunning criminologist. Both were born with cunning, but this characteristic in itself implies no values, neither vice nor virtue. I myself am in possession of a letter from a woman psychologist abroad who wrote to me that her character was down to every detail identical with that of her twin sister. They like the same clothes, the same composers, and the same men. There is just one difference: one sister is full of life and the other utterly neurotic.

As for environment, we know that it does not make man, but that everything depends on what man makes of it, on his attitude towards it. Freud once said: "Try and subject a number of very strongly differentiated human beings to the same amount of starvation. With the increase of the imperative need for food all individual differences will be blotted out, and, in their place, we shall see the uniform expression of the one unsatisfied instinct." But in the concentration camps we witnessed the contrary, we saw how, faced with the identical situation, one man became a swine while the other attained almost saintly status. And Robert J. Lifton (1954, *Amer. J. Psychiat.*, **110**, 733) writes about American soldiers in North Korean prisoner-of-war camps: "There were examples among them both of altruistic behaviour as well as the most primitive forms of struggle for survival."

Thus man is by no means a product of inheritance and environment. Tertium datur: the decision—man ultimately decides for himself! And in the end education is just education towards the ability to decide.

But also psychotherapy must direct its appeal to the ability for decision, to the freedom of attitude. Thus it appeals not only to what we have called man's will-to-meaning but also to the freedom of man's will.

This will cannot simply be derived from the instincts—no more than we can deduce the "should" from the "would". And so we come to the third factor—after the spirituality and the freedom of man: his responsibility. To whom is man responsible? First of all, to his conscience. But this conscience again is also irreducible and indeducible, thus an original phenomenon and no epiphenomenon! One day I was sitting in a restaurant with an internationally famous psychoanalyst. He had just given a lecture and we were discussing it. He was denying that such a thing as a conscience, as an original phenomenon, existed at all, and asked me to tell him what this conscience was. I answered briefly: "Conscience is that which has made you present us to-night with such a splendid

lecture." Whereupon he waxed furious and screamed at me: "That isn't true— I did not deliver this lecture for my conscience, but to please my narcissism!"

To-day modern psychoanalysts themselves have come to the conclusion that "true morality cannot be based on the concept of a super-ego" (Weiss, F. A. (1952) *Amer. J. Psychoan.*, p. 41).

We are thus confronted with two original phenomena which cannot be reduced to other phenomena or rather deduced from them. The first phenomenon was man's freedom, the second man's responsibility. In the face of these two, dynamic or genetic contemplation is insufficient; drives cannot repress themselves. But neither can man be responsible to himself, at least not in the last analysis. Behind his conscience stands, albeit often unknown to him, an extra-human authority. Freud once said: "Man is not only often much more immoral than he believes, but also often much more moral than he thinks." I should like to add that he is often much more religious than he suspects. These days people see more in man's morality than an introjected father-image; and in his religion more than a projected father-image. And they have long ceased to consider religion a general obsessional neurosis of humanity.

I have said that man is often more religious than he himself suspects. But we must not make the mistake of looking upon religion as something emerging from the realm of the id, thus tracing it back again to instinctual drives. Even the followers of Jung have, alas, not avoided this error. They reduce religion to the collective unconscious respectively to archetypes. Once I was asked after one of my lectures whether I did not admit that there were such things as religious archetypes, since it was remarkable that all primitive peoples ultimately reached an identical concept of God, and this could after all only be explained with the help of a God-archetype. I asked my questioner whether there were such a thing as a Four-archetype. He did not understand immediately, and so I said: "Look here, all people discover independently that two and two make four—perhaps we do not need an archetype for an explanation—perhaps two and two really do make four. And perhaps we do not need a divine archetype to explain human religion either—perhaps God really does exist."

There is, ultimately, no such thing as repression of drives by themselves, just as there is no such thing as responsibility to oneself; we can only be responsible to an entity higher than ourselves, and, if we derive the ego from the id and the super-ego from the id and the ego, what we achieve is not a correct picture of man but in some way a caricature of man. This sounds like a tall story of Baron Münchhausen with the ego pulling itself out of the bog of the id by its own super-ego shoelaces.

There is a danger that we may corrupt a man, that we may work into the hands of his nihilism and thus deepen his neurosis if we present him with a concept of man which is not the true concept of man; if we make man into a homunculus. The modern homunculus is not produced in the alchemist's vaults and in retorts, but wherever we present man as an automaton of reflexes, as a mind-machine, or as a bundle of instincts, as a pawn of drives and reactions, as a mere product of instinct, inheritance, and environment.

It occurs, in short, whenever we draw from biological data conclusions which are solely biologistic, from psychological data, psychologistic conclusions.

I became acquainted with such biologism in my second concentration camp, in Auschwitz. For that is where biologism led to, right into the gas chambers of Auschwitz, that was the ultimate consequence of the theory that man is nothing but a product of inheritance and environment, or, as they liked to say in those days, of "Blood and Soil". I am absolutely convinced that the gas chambers of Auschwitz, Treblinka and Maidanek, were ultimately not prepared in some Ministry or other in Berlin but rather at the desks and in the lecture halls of nihilistic scientists and philosophers.

Section of Surgery

President—Sir HENEAGE OGILVIE, K.B.E., D.M., M.Ch., F.R.C.S.

[*March* 3, 1954]

DISCUSSION ON THE NUTRITION OF THE SURGICAL PATIENT

Mr. L. P. Le Quesne (The Middlesex Hospital, London):

By far the commonest type of case we meet with in general surgical practice which presents severe nutritional problems is the patient with gross, organic disease of the alimentary tract, whose disease prevents adequate replenishment by oral feeding and who probably requires surgery in the immediate future. Obvious examples of this class of case are provided by patients with malignant disease of the upper alimentary tract. Thus of the last 16 cases of carcinoma of the stomach or œsophagus admitted to the Department of Surgical Studies, the Middlesex Hospital, 6 have required preparation for operation by intragastric tube feeding, and 4, or one-quarter, by intravenous fluids, and it is this latter type of case which I shall discuss.

In these patients the nutritional disturbance arises from a combination of deficient intake of all constituents of the diet, together with abnormal and excessive losses from vomiting, diarrhœa or fistula formation. These events may easily, and frequently do, lead to a markedly adverse balance in the patient's fluid, electrolyte, protein and calorie exchange. Each one of these deficits is, in itself, highly undesirable and leads to a whole series of events which are prejudicial to the patient's ability to withstand illness and operation. However, they fall into two contrasting groups in that deficits of fluid and electrolytes readily give rise to an obviously serious condition which can be rapidly fatal, but yet which can be corrected comparatively quickly and simply, and furthermore which must be corrected at least in part if surgery is to be carried out successfully. On the other hand, the effects of a protein and calorie deficit are much more insidious in their development and manifestations, are frequently only corrected with difficulty and over a period of time, and in many cases can be neglected with apparent impunity. In practice it is necessary to deal with these equally important aspects of the problem together, but for purposes of discussion it is simpler to separate them, and whilst later speakers will deal with the problem of protein and calorie administration, I will confine my remarks to the management of disturbances of fluid and electrolyte balance before and immediately after operation, disturbances, which to my mind, constitute the most urgent nutritional challenge in this type of case.

The first step in the preparation for surgery is obviously the diagnosis of the presence of a deficiency, followed by an estimation of its size, and of the extent to which water and the various electrolytes contribute to this deficit. In the great majority of these cases the fact that a deficit exists is immediately apparent, but it is important to be constantly on the look-out for less obvious but none the less serious deficiencies in any patient who has an interference with his normal intake or who has abnormal losses. No elaborate investigation is needed to disclose such a deficit, and if there is any doubt the point can be settled with certainty by keeping an accurate intake and output chart for twenty-four to forty-eight hours.

However, though the recognition of the presence of a deficiency is simple, it is unfortunately not so easy to arrive at an accurate assessment of its size or the degree to which water or salt, that is sodium, depletion contributes to the whole picture. At the moment there is no one single test simple enough for routine clinical usage which will give a reliable estimate of the size of the deficit, and such an estimate can only be arrived at by a careful consideration of the available clinical and biochemical evidence. In assessing this evidence it is important to bear in mind the size of the fluid compartments in the body with which we shall be dealing and also the fundamentally different effects of sodium and water depletion. Fig. 1 shows the main facts of the distribution of body water in an unusual form. The normal daily exchange of water is equal in amount to one-seventh of the extracellular space, and daily there is secreted into the alimentary tract some 8 litres of digestive fluids containing an essentially isotonic concentration of electrolytes; it is thus apparent that we may easily see patients with a deficit amounting to several litres of water and saline.

Whilst this figure suggests that the composition of the various body spaces differs, it does not perhaps emphasize this enough when we recall that the intracellular fluid has as its main ions potassium and phosphate, in contrast to the presence of sodium and chloride in the extracellular space, from which it is separated by a membrane freely permeable to water but relatively impermeable to electrolytes. Nor does this picture remind us of the fact that one of the most important properties of these fluids is their osmotic pressure, which the body guards most zealously, so conferring on the irreplaceable sodium ion a dominant position in the body economy. It is this over-riding importance

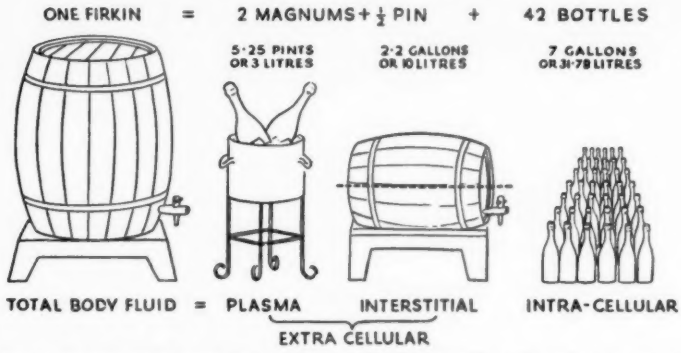
ONE FIRKIN = 2 MAGNUMS + ½ PIN + 42 BOTTLES
5·25 PINTS OR 3 LITRES
2·2 GALLONS OR 10 LITRES
7 GALLONS OR 31·78 LITRES
TOTAL BODY FLUID = PLASMA INTERSTITIAL INTRA-CELLULAR
EXTRA CELLULAR

FIG. 1.—Illustrating the volume of total body water and its distribution in the various body compartments (Reproduced from "A Medical Bulletin", July 1953, by kind permission of Messrs. May & Baker Ltd.)

of the maintenance of isotonicity which leads to the well-known and fundamental difference between the effects of water and salt, or, more accurately, sodium depletion. This difference is illustrated diagrammatically in Fig. 2, which shows that water depletion initially causes hypertonicity in the extracellular space, but that this is compensated for by a shift of water from inside the cells resulting in essentially intracellular depletion, whereas in contrast salt depletion by similar processes results in extracellular depletion.

Recent work shows that this explanation is too mechanistic, but nevertheless it forms an essential concept in interpreting problems arising in clinical practice. For though we rarely see pure water or salt depletion states, the complex picture that is presented by the usual mixed syndrome is compounded essentially of the effects of these two conditions, and we can achieve an assessment of the type and extent of the depletion by dissecting out from the whole picture the effects of each. These effects can be seen on clinical examination and by analysis of the blood and urine, and are diagrammatically shown in Fig. 3. Here the two compartments represent the two components of the extracellular space, the intravascular space or plasma, and the interstitial space, the two differing in composition only by the presence of protein in the former. Water depletion, as we have seen, causes little or no diminution in the size of the extracellular space, so that the concentration of protein and electrolytes will be normal until late in the condition when both will show a progressive rise: the urine output will, of course, be very low with a urine of high specific gravity and salt concentration, the latter usually being measured in the form of chlorides. In contrast to this picture, the contraction in salt depletion largely affects the extracellular space, and in particular the interstitial space as the osmotic force

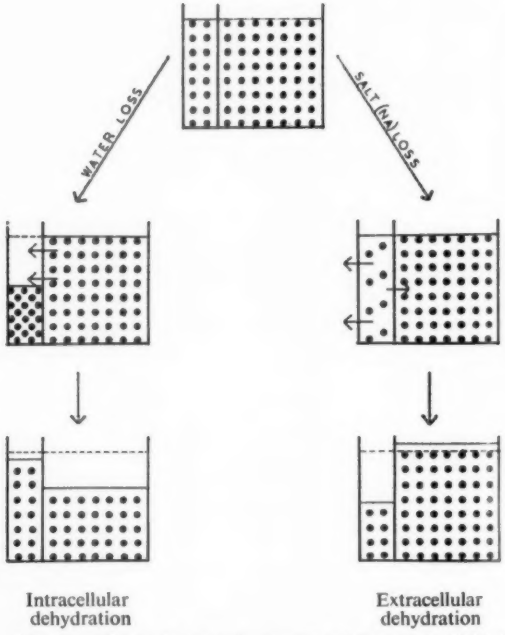

FIG. 2.—The body water is represented as a tank, divided into two portions representing the intra- and extracellular compartments: the concentration of electrolytes is shown by the dots. Water depletion initially causes extracellular *hypotonicity*, which is compensated for by a shift of water out of the cells leading to *intracellular dehydration*. Salt depletion initially causes extracellular *hypotonicity*: in the main this is compensated for by an excretion of water, leading to *extracellular dehydration*. (Reproduced from the author's "Fluid Balance in Surgical Practice", 1954, by kind permission of Messrs. Lloyd-Luke (Medical Books) Ltd.

of the plasma proteins maintains the plasma volume until late in the condition, when a steadily falling circulating volume will lead to postural hypotension and eventually the full-blown picture of peripheral circulatory failure. This fall in the plasma volume is reflected by a rising protein concentration and hæmoglobin figure, though the plasma electrolyte figures will only fall late in the condition. Assuming the water intake is normal the urine in pure salt depletion will be copious and of low specific gravity, but its main feature will be the complete absence or very low concentration of salt (usually measured as chlorides). As well as these biochemical differences the two conditions present markedly different clinical features. In water depletion thirst is present and prominent but there are few clinical signs. In pure salt depletion thirst is absent, but the patient feels lethargic and drowsy, the skin is dry and lacking in its usual elasticity, and as the condition develops there will be postural hypotension followed by vomiting and a state of peripheral circulatory failure indistinguishable from shock. The occurrence of these last two symptoms as a result of salt depletion needs emphasis, as a failure to recognize their true cause may lead to serious mistakes in treatment.

The problem, then, in a typical case of mixed deficiency is to isolate from the whole picture the telltale signs of these two basic depletions. The patient's story may help considerably by indicating the length of time over which the intake has been absent or inadequate, and some idea of the quantity and nature of abnormal losses, whilst the clinical examination may reveal some or all of the signs just

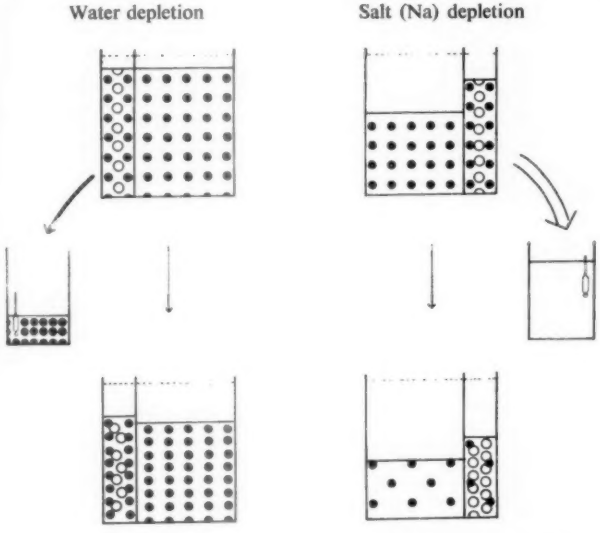

FIG. 3.—Diagrammatic representation of the different effects of water and salt depletion. The two compartments of the tank represent the two components of the extracellular space, namely the extravascular or interstitial space, and the intravascular or plasma space. The dots represent the concentration of electrolytes, and the circles the plasma protein concentration. The urine output is represented by the arrows and containers to either side. See text for full explanation.

Clinical	Thirst	Diminished skin elasticity, &c.: lethargy: postural hypotension: vomiting: peripheral circulatory failure.
Blood	Rising blood urea Rising Hb (late) Rising Na and Cl (late)	Rising Hb and Pl.Pr. Rising blood urea Falling Na and Cl (late)
Urine	High sp. gr.	Low or absent Cl

discussed. When considering the biochemical evidence it is important to concentrate on the essential investigations and usually four simple tests are adequate, namely the urine specific gravity, the urine chloride concentration, the hæmoglobin or plasma protein concentration and the blood urea concentration. A raised urine specific gravity, above 1015 or more, is diagnostic of water deficiency whilst a low or zero urine chloride figure is equally strong evidence of salt depletion, particularly when the urine volume is low. The hæmoglobin or plasma protein figure gives an indication of the degree of hæmoconcentration and so extracellular contraction, and the blood urea concentration is a very sensitive index of depletion as it is raised by either water or salt depletion. It is to be noted that quite severe degrees of depletion can exist with normal concentrations of serum electrolytes and their estimation is not essential except in difficult cases.

Based on this clinical and biochemical examination of the patient it is possible to arrive at an assessment of the extent and nature of the depletion, and in this final analysis it is helpful to remember

that in a patient with moderately severe signs there is probably a deficit of some 3–4 litres, largely extracellular in acute cases but more evenly distributed in chronic states. With this estimate made replacement can now begin, the fluid required being given over and above the basic intake over a period of twenty-four to seventy-two hours depending upon the circumstances. During this period every case should be treated as a therapeutic experiment, and the effects of treatment on the clinical and biochemical changes carefully observed every twelve to twenty-four hours. In this way the initial and subsequent findings gain greatly in significance when assessed in relation to the treatment given and the final stages of replenishment can be accurately controlled. This process of replenishment is complete when all clinical signs of depletion have disappeared, when the blood urea, plasma protein and serum electrolyte concentrations are stable within normal limits, and when the urine volume exceeds one litre per twenty-four hours with normal specific gravity and chloride concentration.

These points are well brought out by Fig. 4, showing the observations made during treatment of a man with severe pyloric stenosis, who was grossly depleted on admission and who had been losing essentially equal amounts of Na and Cl. During the four days needed to effect replenishment he received some 5 litres of fluid daily by intravenous drip, consisting of about equal parts of dextrose and saline. During this replacement there was a weight gain of 14 lb. in four days, indicating that the initial deficit was in the neighbourhood of 6 litres, and the upper graph shows the steadily rising urine volume as this water deficit was made up. This rise in urine output was also accompanied by a steady drop in urine specific gravity from 1025 down to a normal figure of 1006, and by a return of the blood urea from the high figure of 50 mg.% down to normal levels (26 mg.%). The lowest graph shows the data relevant to salt depletion: initially there was virtually no chloride in the urine, but gradually both the absolute amount and concentration rose as treatment proceeded, and indeed at one stage the replacement was probably excessive, but both figures were within normal limits after five days. This replacement of salt resulted in a return of the extracellular space to normal size, and this is shown by the steep fall in hæmoglobin concentration, but it is to be noted that even in the presence of such a severe deficit as this there was a relatively minor alteration in the serum chloride concentration. This case illustrates well how, by their repetition, simple observations gain greatly in significance, and enable even large deficits to be successfully assessed and replaced. It is worth noting that the hæmoglobin figures in this case show a fall of some 25% in three days. These patients are frequently not only dehydrated but also anæmic. This anæmia may well be masked initially by the hæmoconcentration and only revealed as treatment proceeds; this should be carefully watched for, so that blood can be given before the hæmoglobin reaches a dangerous level, and in this case the hæmoglobin was only maintained above 80% by giving 2 pints of blood during the third and fourth days.

In my experience it is only rarely necessary to use special solutions to counteract acid-base disturbances, as in most cases the kidneys are capable of making the requisite adjustments. However, many of these cases do require a special solution of another kind, namely potassium. Potassium deficiency occurs most characteristically in the post-operative period, but a significant potassium depletion of some 200–300 mEq. may easily be seen under the conditions being discussed and its replacement is important, though this should not be started on until the major deficit of water and salt has been largely replaced, and until the urine output has been restored to at least 1 litre per twenty-four hours. At this stage the need for potassium can be gauged by estimation of the serum K concentration and by looking for the changes of K deficiency in an ECG tracing. If potassium is required and must be given intravenously it is wise not to exceed a total daily dosage of 80 mEq., that is the amount contained in 6·0 grams of potassium chloride, and this should not be given at a rate in excess of 20 mEq./hour. We have used extensively a solution containing 40 mEq. K, that is 3·0 grams KCl, per litre of 5% dextrose. Concentrations higher than this are painful to administer and possibly dangerous, but we have seen no ill-effects from this solution.

Whilst it is usually not too difficult to correct the various deficits in the manner described, the maintenance of equilibrium by intravenous routes for any length of time requires delicate biochemical juggling, and necessarily involves an increasing calorie and protein deficit. This latter point was well illustrated by one of our patients who, in the nine days spent preparing him for operation, lost 22·7 grams of nitrogen, which is equivalent to 715 grams of beefsteak. Accordingly, unless feeding into the alimentary tract can be established in some way, it is important to proceed with surgery promptly. Now, during recent years many very abstruse articles have been written about the endocrine changes which occur after operation and their effect upon the administration of fluids. There is no doubt that the subject is a complex one and much is still obscure, but the essential core of the situation is quite plain. After operation there is a metabolic disturbance, apparently in the main due to an increased secretion of adrenocortical hormones and of the anti-diuretic hormone, resulting in an increased urinary excretion of nitrogen and potassium, and, of far more importance, a marked depression of the kidney's ability to excrete water and salt (Le Quesne, 1953). Fig. 5 shows the urinary output for successive four-hour periods from a patient undergoing a sigmoid colectomy, who received an absolutely constant intake of water and electrolytes for forty-eight hours before and after operation. It can be seen how operation is immediately followed by a profound fall in the rate

of urine flow which lasts for thirty hours after operation, and which is accompanied by a synchronous rise in urine specific gravity. Usually this inability of the body to eliminate water normally lasts some thirty-six hours after operation, but the impairment of salt excretion is much more prolonged, lasting

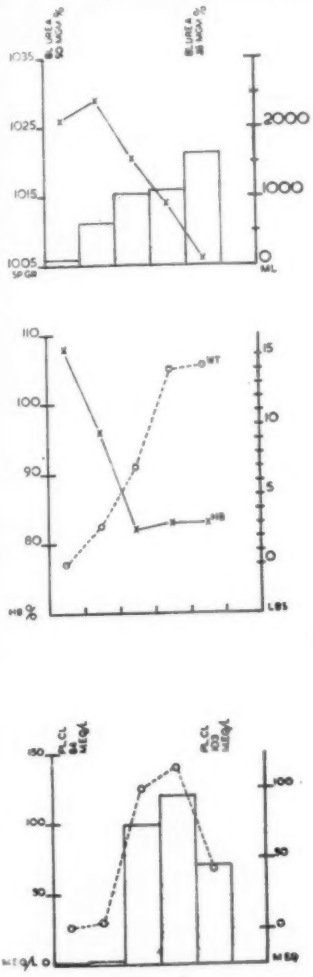

FIG. 4.

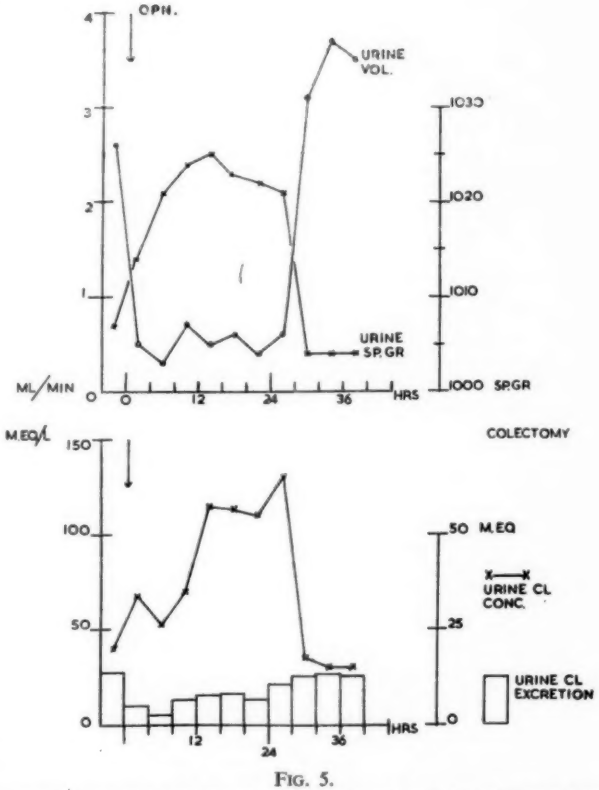

FIG. 5.

FIG. 4.—Data obtained during course of treatment of a patient with severe water and salt depletion resulting from pyloric stenosis. The upper graph shows the daily urine output (blocks) and the urine specific gravity (crosses). In the centre graph the daily body-weight and hæmoglobin figures are recorded. The lowest graph shows the daily, absolute urine chloride output (blocks) and the daily urine chloride concentration. *See* text for further details.

FIG. 5.—Data from a patient undergoing sigmoid colectomy, who received a constant intake of water and electrolytes for forty-eight hours before and after operation. For thirty hours after operation there is a profound fall in the rate of urine flow, which is accompanied by a synchronous rise in urine specific gravity. The lower graph shows that during this period of diminished urine flow the urine chloride concentration is raised, though the absolute excretion of chloride falls off (Reproduced from the author's "Fluid Balance in Surgical Practice, 1954", by kind permission of Messrs. Lloyd-Luke (Medical Books) Ltd.).

five to six days after major surgery. Fig. 6 again shows observations made on a patient receiving a constant intake of water and salt before and after operation, and demonstrates the falling off in the absolute secretion of sodium for four days after surgery, with the accompanying fall in the urine

sodium and chloride concentration. The important practical significance of these changes lies in the fact that if too much glucose or saline is given after operation the excess cannot be excreted from the body but is retained, and in extreme cases this can lead to water intoxication or obvious œdema formation. There is considerable disagreement as to the optimal requirements of salt and water during this period, but it is important not to overdo our zeal for avoiding these dangers of overloading and to provide an intake which will allow some small margin for the various increased losses which occur so commonly after major surgery. During the first twenty-four to forty-eight hours after operation the depression of water excretion is so marked that it is probably wise not to give more than 2 litres per twenty-four hours, though thereafter the limit may be raised to 3 litres per twenty-four hours. With regard to salt, the amount contained in one half-litre of normal saline, that is 80 mEq. or 4·5 grams NaCl, is quite adequate and does not provide sufficient to allow of dangerous retention, but in any twenty-four hours this amount should not be exceeded unless there are abnormal losses. During the last two years it has been my habit to add to this intake, after the first thirty-six hours after operation, 80 mEq., that is 6 grams, of KCl, each twenty-four hours, and whilst I do not suggest this is essential I am sure that, if carefully controlled, it is most valuable in preventing the development of hypokalæmia.

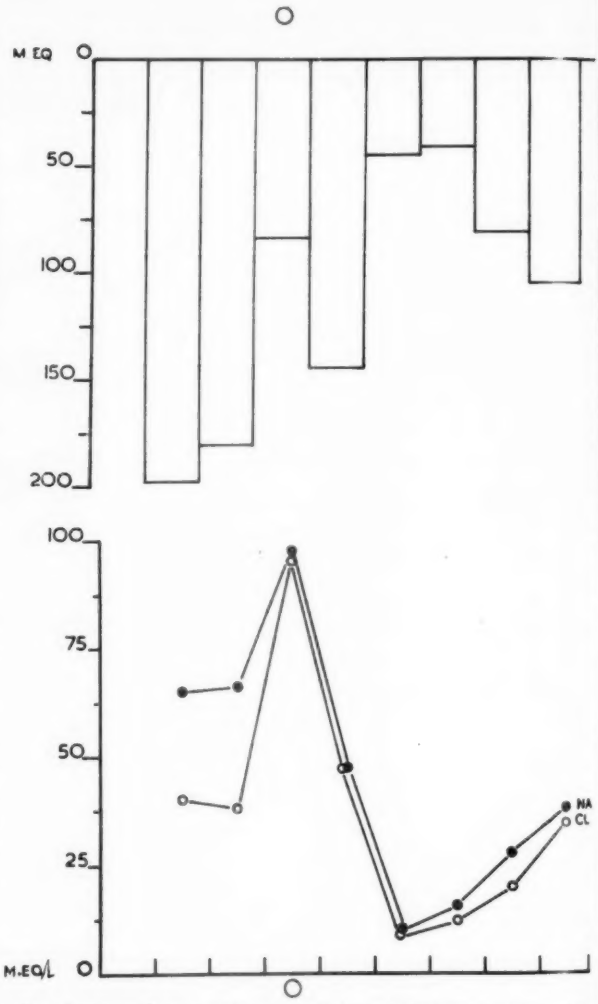

FIG. 6.—Data from a patient undergoing subtotal gastrectomy who received a constant intake of water and electrolytes throughout the period illustrated. The upper, "stick" graph shows the urinary sodium excretion each twenty-four hours: following operation (O) this is diminished for six days, with the minimum excretion occurring on the third post-operative day. This period of diminished excretion is accompanied by a markedly lowered concentration of sodium and chloride in the urine, as shown by the lower graphs.

For twenty-four to forty-eight hours after operation the post-operative metabolic changes necessarily lead to a urine of raised specific gravity and similarly during the second to fifth days they cause a distinctly lowered urine chloride concentration. It is most important that during this period these changes should be recognized for what they are, and not taken as indicating a shortage of water or of salt, as this can lead to gross overloading.

It is my experience that in the majority of cases it is unnecessary to burden the biochemical department with extensive investigations, and these concepts give most valuable guidance for the management in the ward of these often difficult cases.

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Mr. **R. H. F. Brain** (Guy's Hospital, London): Among the many aspects of surgical malnutrition there is one which has received less attention than it deserves—namely chronic solid depletion. Recently I have made certain metabolic observations in cases illustrative of this problem.

Throughout I have tried to study, in particular, patients in the pre-operative phase who tend to develop nutritional defects as a result of surgery. I refer to the radical œsophagogastric resections and their complications (Brain and Stammers, 1951; Brain, 1953). I have also used certain potent metabolic materials like ACTH, testosterone, and the antibiotics as aids in nutritional rehabilitation.

The use of ACTH for this purpose may at first sight seem rather contradictory, since its known effects are mainly anti-anabolic, leading to a breakdown of tissue protein and a negative nitrogen balance. Nevertheless, its beneficial effects in promoting a general feeling of well-being, increasing the appetite and thereby increasing the calorie intake are well known and have been successfully utilized in elderly people (Cole, 1953). Testosterone therapy would appear to be founded on even better grounds as its effect is definitely anabolic. The antibiotics in small doses are apparently paying large dividends in growth and increases in weight in the agricultural world (Agricultural Research Council, 1953) and are therefore worthy of our trial for this purpose.

Causes of malnutrition.—Malnutrition in my practice is common and is seen in association with many disorders, such as obstructive states of the upper alimentary tract, severe infections like empyemas and subphrenic abscess, and neoplastic disease. In this last condition the effects are frequently multiple and may include a limitation of food intake, losses from diarrhœa or secondary sepsis, often an increased demand for food due to the growing tumour itself; Bateman (1950) has assessed this at 60% to 90% of the total nitrogen utilization in certain cases. New growth also may affect vital nutritional areas like the liver or the suprarenals especially where actual secondary invasion has taken place. Lastly I recognize chronic anoxia as a common cause of undernutrition. Chronic pneumothorax, many patients with mitral stenosis and, of course, blue babies are excellent examples of this. Campbell and Reynolds (1949) comment that in congenital cyanotic heart disease the average individual is only 77% of normal weight and that this is invariably associated with a very poor appetite.

I have selected anoxia for rather special mention, because I think that it has been perhaps neglected and also because it carries with it the useful corollary of demonstrating how important an adequate oxygen supply is for good nutrition. Anoxia by causing a loss of gastric tone with delayed emptying of the stomach leads to anorexia, while its effect on general tissue oxidation produces at least a depression of tissue function, sometimes degeneration and even necrosis. Any one of the classical causes of anoxia may contribute to undernutrition but undoubtedly the commonest and therefore the most important is anæmia which imposes at least a double burden on nutrition: firstly by being associated with the general effects of anoxia and secondly because of the fundamental raw materials like nitrogen and potassium which are required by the bone-marrow to rebuild the red blood cells. Moore (1949) has stressed this point.

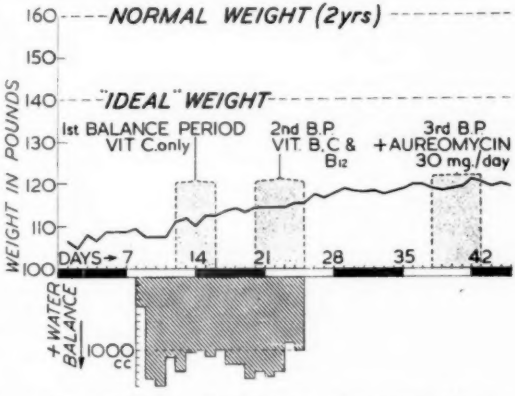

FIG. 1 (*Case I*).—Weight chart. Carcinoma of œsophagus with secondaries. Basal calories—1,500/day. Diet.—3,000 c./day. Protein—128 grams. Fat—100 grams. C.H.—397 grams.

Surgeons have long recognized the beneficial effect of giving blood transfusions to poor surgical risks. Indeed so impressed have I been that it is my practice to give one, two, or even three pints of blood to such cases, even where no actual anæmia exists but where the general nutritional state requires boosting.

General surgical fitness and the importance of the building up of a nutritional reserve.—It is, of course, a well-recognized fact that the previously healthy and fit patient withstands the trauma of operation, the burden of tissue repair and, if necessary, a modicum of post-operative trouble with the greatest ease. Conversely we all know that patients with severe nutritional deficiency, be it solid, fluid, or a combination of both, are poor surgical risks with a higher initial mortality, they tend to heal poorly and to recover more slowly. This, however, is of course by no means always the case, many of us have seen the most gratifying recoveries from such poor risks.

We are indebted to workers in this field like Moore and Ball (1952) for the recognition of different types of nutritional response to surgery, the important one for us to consider now is the so-called "predepleted response" which constitutes a small negative nitrogen balance following operation together with a less well-marked potassium negative balance and a potassium/nitrogen ratio approxi-

mating to that found in the body tissues. This response contrasts with what we must recognize as the natural catabolic reaction to surgery which, initiated by the suprarenals, results in a generous breakdown of body tissue, and thus the release of the fundamental materials required for healing &c., and which, incidentally, makes the individual quite independent of food intake during this period, a fact pointed out by Albright and Reifenstein (1948). In other words if the subject is poor nutritionally, then the natural catabolic response will be a small or a minimal one which conserves tissue but often to the detriment of a rapid and satisfactory recovery.

This, therefore, is the main reason why an adequate nutritional reserve is necessary, and why it is highly desirable to replenish depleted subjects whenever possible before surgery.

The problem of replenishment.—The provision of a complete and balanced diet is obviously necessary. When constructing such a diet one should have in mind the following fundamental issues:

(1) An adequate intake of calories, since these act as fuel for metabolic energy, "sparers" of the nitrogenous foods, and as materials utilized for the building-up of a calorie reserve in the form of fat.

Calories are available in all the basic food materials. Unfortunately carbohydrates cannot be stored as glycogen in amounts greater than will be required by the body for twenty-four hours, while the use of protein for this purpose is wasteful especially when it is endogenously supplied. We are left, therefore, with fat as the only means of storing calories, and although many people, among them surgeons, consider fat patients a nuisance and poor surgical risks, for myself I find that they tolerate major surgery often very much better than their thin counterparts. Recently I have had an excellent illustration of this when a fat male patient of 74 years weighing 13½ st., underwent an almost total œsophagectomy, made a perfect recovery, was eating quite well by the fifth day after operation, yet he lost 1½ st. by the end of the third week. This loss, of course, he could very well afford, and in doing so provided himself with a considerable number of valuable calories.

For my patients I provide calories in amounts equal to double their basal requirements based on their ideal weights. They have usually been provided by mouth, otherwise by gastrostomy, rarely by jejunostomy, and never intravenously since, as glucose, it is impossible to provide the large number required without incurring considerable losses from spill-over into the urine. The intravenous fat emulsions of Stare and used by Shafiroff *et al.* (1949) have an obvious place here but, so far, they have not been available to me.

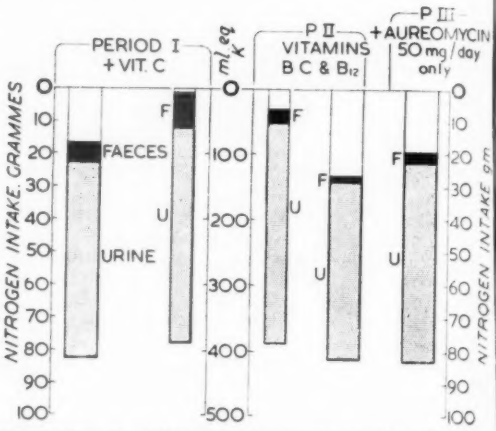

FIG. 2 (*Case I*).—Nitrogen and potassium balance (4 day).

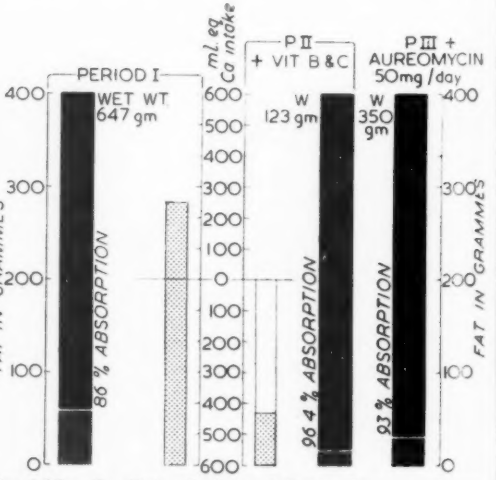

FIG. 3 (*Case I*).—Fat and calcium balance. Carc. œsophagus and gastrostomy. Diet. Fat—100 grams. Cal.—3,000.

(2) It is essential to provide sufficient nitrogen in the form of protein. I have already laid some stress on its importance in the adaptive, healing, and rebuilding processes after surgery. Nitrogen is available in reserve in the form of the general musculature. Howard states that the compulsory negative balance after operation may run as high as 16 grams a day and may last up to ten days (Howard *et al.*, 1946).

I have provided protein in amounts equal to 1·5 to 2 grams/kilo of their ideal weight, that is about four times their basic requirements. They have usually been given by mouth in liquid form as milk protein and hydrolysates. Only very occasionally have I used the intravenous route for the giving

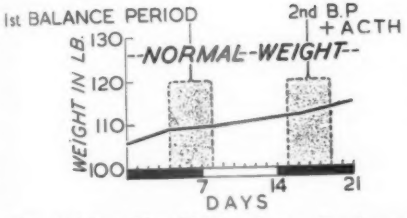

FIG. 4 (*Case II*).—Weight chart. Carcinoma of œsophagus with secondaries. Basal calories −1,360/day. Diet−2,720 c./day: Protein−100 grams. Fat−100 grams. C.H.−340 grams.

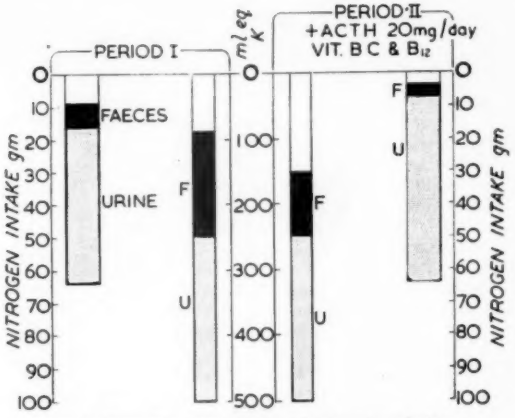

FIG. 5 (*Case II*).—Nitrogen and potassium balance (4 day).

of protein since it provides so many difficulties, the amino-acid solutions seemingly suffering from a high loss rate in the urine, while opinions as to the nutritional value of plasma vary, Moore stating that its benefit is solely an osmotic one, whilst Hawkins and Whipple (1938) disagree stating that since there is no latent loss of nitrogen it must therefore be metabolized. Probably both are correct, the "time factor" leading to this difference of opinion.

(3) All accessory factors such as the vitamins, especially vitamins B and C in saturation doses are provided. I recently saw a lady with an œsophageal carcinoma who presented herself as a case of frank scurvy, thus emphasizing the severity of the depletions that may occur in such cases.

(4) Finally, special care was taken to see that patients on forced feeding had exercise and general physiotherapy to develop their muscles, because immobilization and rest in general lead to wasting and nitrogen loss, and activity to an accumulation of a reserve.

The following cases of pre-operative surgical malnutrition are taken from among those who have recently had relevant metabolic studies and demonstrate many interesting points.

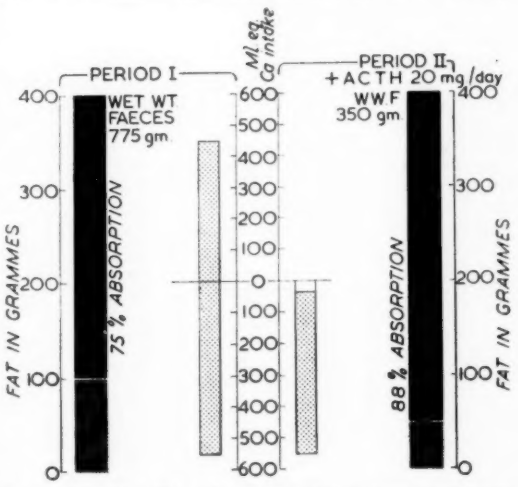

FIG. 6 (*Case II*).—Fat and calcium balance. Carc. œsophagus and gastrostomy. Diet. Fat−100 grams. Cal.−2,720.

Case I.—Mr. T., a 68-year-old man, presented originally with a metastatic carcinomatous gland in his neck for which no primary site could be found. Dysphagia developed eighteen months later and was quickly followed by a severe weight loss of 65 lb. Further investigation revealed a mid-third œsophageal growth. Intubation having failed, a feeding gastrostomy was done with a view to relieving his dysphagia later with an œsophago-jejunostomy.

Metabolic study showed that despite the rapid development of further metastases he steadily put on weight (Fig. 1). His nitrogen and potassium balances during each of three different periods were satisfactorily positive and varied very little with the differing medical agents given during these periods (Fig. 2). His fat and calcium balances are of interest since in the first period he has a mild steatorrhœa associated with a large negative calcium balance, whereas in his second study period a week later a normal absorptive figure is shown, in association with a satisfactory positive calcium balance. Normal figures are shown in his third period (Fig. 3).

Case II.—Mr. D., aged 72 years on admission to Guy's Hospital, had suffered from dysphagia for three months, he had lost 28 lb. in weight. His general condition was very poor due to a mid-third carcinomatous stricture of his œsophagus which proved to be impassable at œsophagoscopy. A gastrostomy was performed because it was felt that his general condition could be improved sufficiently to allow a thoracotomy to be done later.

This view was amply justified as on a 2,720 calorie diet he put on 12 lb. in the following three weeks (Fig. 4). Balance studies during two periods show a satisfactory nitrogen and potassium positive figure (Fig. 5). It is of interest that the effect of ACTH during the second period was to reduce the positive nitrogen balance while increasing that of potassium. The use of ACTH here is almost certainly pointless since its general effects of increasing appetite, &c., were rendered ineffective by his gastrostomy and fixed calorie intake. Similar changes in his fat and calcium balances during the two periods are seen to those in the first case, namely a mild steatorrhœa with a large negative calcium balance in the first period, followed by a fat absorption approaching normal and with a small positive calcium balance in the second (Fig. 6). Viewing these results critically it must be pointed out that the wet weight of fæces analysed in the two periods was very different being 775 in the first and only 400 in the second despite the careful marking and collecting of the stools. Subsequent thoraco-abdominal exploration showed him to be inoperable because of liver secondaries, nevertheless he stood a palliative œsophago-jejunostomy very well.

Case III.—Mr. E., aged 71 years, was admitted with a four-months' history of severe anorexia, dyspnœa resulting from his anæmia, and a weight loss of over 28 lb. due to a massive prepyloric carcinoma of the stomach.

Attempted nutritional rehabilitation by transfusions and an increased diet failed because it was quite impossible to raise his caloric intake above 1,600/day whereas his basal need was 2,094/day, consequently as can be seen in Fig. 7 he continued to lose weight steadily. A nitrogen balance during this period (Fig. 8) was negative as could be expected from his low calorie intake, surprisingly his potassium balance was still just positive. He also had the moderate steatorrhœa that we have learnt to expect in such cases.

It was felt that his general condition was far too poor for a gastrectomy, consequently three weeks after his admission a gastro-enterostomy was performed under local anæsthesia with a view to increasing the calorie intake and thereby improving his nutritional state prior to a radical excision. Unfortunately he was still unable to cope with an increase in his diet despite his functioning gastro-enterostomy, so that he continued to lose weight and strength. Occasional vomiting and the persistence of his severe anorexia account for this failure and probable result from the combined effects of the growth itself and his chronic anoxic state. The latter followed on his severe anæmia which persisted despite transfusions and was due to the steady loss of blood from the surface of his ulcerating carcinoma.

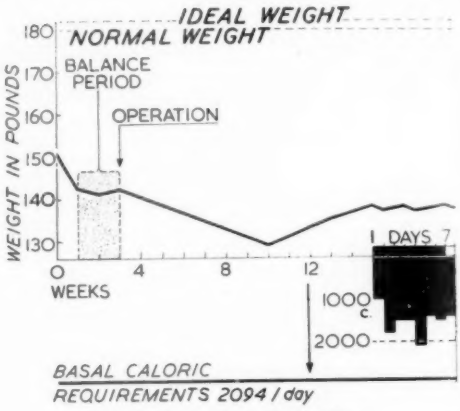

FIG. 7 (*Case III*).—Weight chart.

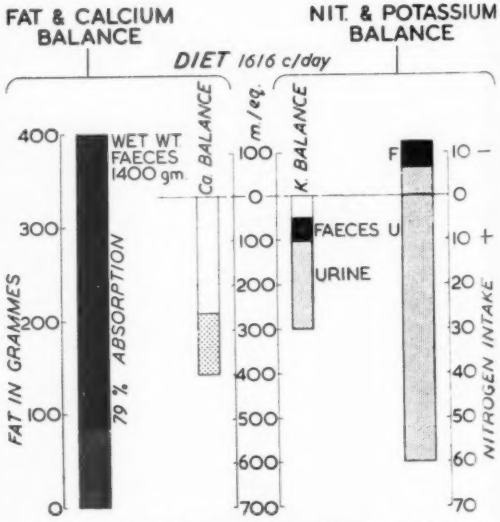

FIG. 8 (*Case III*).—Metabolic balances. Carc. stomach with severe anæmia.

Case IV.—Mr. A., a 56-year-old man, presents a problem of nutritional œdema, a condition not uncommon as a transient feature in thoracic surgical cases, particularly after major operations like pneumonectomy.

His only symptoms of a carcinoma of lung were anorexia, and loss of weight of 3½ st. Following a lobect my

he developed an empyema which was drained. He continued to do badly and became œdematous despite an apparently adequate calorie and protein intake. Study revealed a small negative nitrogen balance entirely as a result of pus formation (*see* Fig. 9); his serum proteins were reduced. Despite limitation of his fluid and electrolyte intake his œdema became steadily worse, while his serum albumin fell to 1·8 grams. Repeated massive plasma transfusions of 1,000 c.c./day were used in an attempt to rehabilitate him, as recommended by Allen *et al.* (1950): however, after two such transfusions on successive days he suddenly developed acute pulmonary œdema and died. There had not been a diuresis or a change in his serum protein level.

Post-mortem showed an acute liver necrosis. I wish to draw attention to this danger following massive plasma therapy and which is perhaps more likely to occur in patients having an impaired liver function.

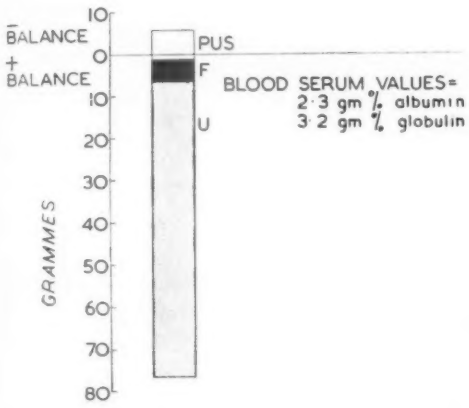

FIG. 9 (*Case IV*).—Nitrogen balance. Empyema. Nutritional œdema. Diet—2,300–2,900 c/day. Protein 100 grams/day.

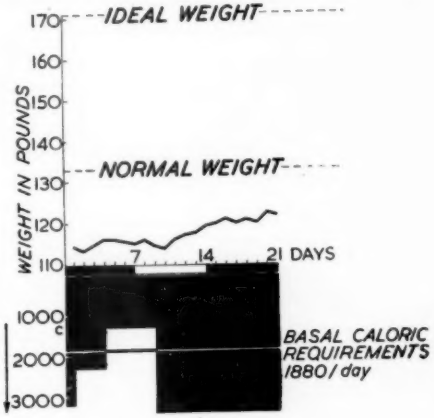

FIG. 10 (*Case V*).—Weight chart.

Case V.—Mr. N., aged 49 years. Large carcinomatous lung abscess, and a loss of weight of 20 lb. in a short time. His severe wasting was due, at least in part, to a continuous pyrexia and the excretion of large amounts of pus as sputum each day.

Rehabilitation was commenced using blood transfusions and a high calorie diet. At first he found his diet very difficult and sometimes impossible to take, later with improving health it became noticeable that his appetite was returning and that now he was enjoying his food. He soon began to put on weight and by the end of the third week he had gained 10 lb. and was considered fit for operation (Fig. 10).

Unfortunately at operation it was impossible to remove his growth, and he was discharged home.

Case VI.—Mrs. M., aged 32 years, also presented herself to us principally as a case of severe malnutrition consequent upon a weight loss of 40 lb. in one month after the drainage of a right suprahepatic subphrenic abscess. At the time of the drainage her pleura had been opened so that she had a tension pyopneumothorax in addition. The combined effects of severe sepsis, anoxia and anorexia were, no doubt, responsible for her weight loss.

Successful solid rehabilitation followed the deliberate raising of her caloric intake, the appetite again noticeably improving with weight gain (*see* Fig. 11).

A successful decortication of the right lung was done three weeks following her admission to hospital.

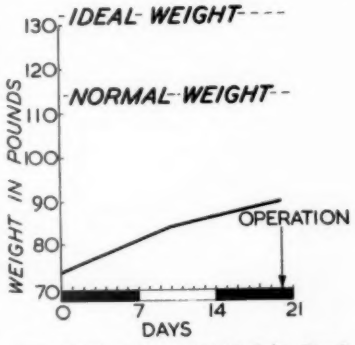

FIG. 11 (*Case VI*).—Weight chart. Basal caloric requirements—1,650 c/day. Diet—2,900 c/day.

Assessment of nutritional fitness for operation.—When assessing my patients prior to operation I rely on:

A progressive increase in weight, providing that it is truly "solid". The daily weighing of the patient seems to be a simple way of assessing the reserve that has been built up. If we accept the figures of Strang *et al.* (1935) (75% fat and 25% protein as the composition of the tissue stored in response to adequate feeding following simple starvation) then for each pound of tissue stored 16 grams of nitrogen becomes available. This would provide catabolic nitrogen in the post-operative period for from one to three days, depending upon the reaction of the individual, and as this period

lasts on an average from three to seven days, the possible maximum requirements of rebuilt tissue would seem to be about 7 lb. Of course this is pure supposition on my part, especially as one is comparing non-pathological cases of simple starvation with complex surgical cases. Nevertheless I like to see undernourished patients put on at least half a stone in weight before operation.

An improvement in the general well-being of the patient and especially in the appetite is obviously a good sign. An interesting clinical fact that has been noticed is that often after quite a short period of forced feeding many undernourished patients find a renewed interest in food.

Unlike other writers I have not been impressed by the serum protein levels as indicators of the state of the nitrogenous reserve, since in surgical patients these may be affected by other factors such as their state of hydration or their liver function.

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Dr. W. H. H. Merivale (Reader in Clinical Pathology, Guy's Hospital Medical School):

The Treatment of Disorders of Acid-base Balance and Potassium Deficiency

Introduction.—It is the purpose of this paper to discuss the acute nutritional disorders which result in alterations of acid-base balance of the extracellular fluid in surgical patients before or after operation, and to indicate methods of treatment which have proved reasonably successful.

Material.—The paper is illustrated by reference to the clinical course and biochemical investigations on which treatment was based of a woman with bicarbonate depletion due to loss of pancreatic secretion, and a man with hypochloræmic alkalosis and potassium depletion due to vomiting from pyloric stenosis. Neither patient was considered as a research problem, and the investigations were made as part of routine work done on them, so that rational replacement therapy might be prescribed.

Methods.—Biochemical investigations were made by routine methods (King, 1951) and in all cases the sodium and potassium content of plasma, gastro-intestinal secretions and urine was estimated by flame-photometry.

RESULTS

Case I. Mrs. C., aged 27. *Estimated body weight* 50 *kg.*

For seven days before beginning rational replacement therapy this woman had been losing between two and three litres of mixed bile and pancreatic secretion every twenty-four hours. She had been treated with intravenous infusions of sodium chloride which had kept her in fluid balance and prevented her from developing either sodium or chloride depletion. On the day on which rational replacement was started (Day 0, Diagram 1), her plasma bicarbonate was grossly reduced, at 5·6 mEq. per litre, and her plasma sodium level was 176 mEq./l., which was probably falsely high due to mixture of a small amount of blood obtained with the heparin used as an anticoagulant. Clinically she was not dehydrated nor particularly thirsty, and she did not complain of the fatigue and weakness which is often characteristic of potassium depletion. Her skin was slack and colourless, and her eyes lacked lustre and life. She looked and felt very ill. There was no tetany.

It was decided to change over from intravenous sodium chloride to $\frac{1}{6}$ molar sodium lactate solution. This would replace the bicarbonate of the pancreatic component of the mixed secretion which she was draining. The amount she needed was calculated from her plasma bicarbonate level and her estimated weight as follows:

Plasma bicarbonate	5·6 mEq./l.
Lower limit of normal plasma bicarbonate	25 mEq./l.
Therefore deficit	25–5·6 or 19·4 mEq./l., say 20 mEq./l.
Estimated body weight	50 kg.

4·2 ml. $\frac{M}{6}$ sodium lactate solution per kg. body weight will raise the plasma bicarbonate level by 1 mEq./l.

Therefore for this patient $4{\cdot}2 \times 50$ ml. $\frac{M}{6}$ sodium lactate would be needed to raise the plasma bicarbonate by 1 mEq./l., and $4{\cdot}2 \times 50 \times 20$ ml. (4,200 ml.) would be needed to bring her plasma bicarbonate concentration up to the lower limit of normal, without in any way replacing the continuing losses in the drainage fluids.

In the first forty-eight hours of replacement she received 582 mEq. bicarbonate (Diagram 1. Days 0 and 1) as sodium lactate intravenously, and lost 199 mEq. most of which was contained in the drainage fluid, since there was practically none in her urine. On Day 2 her plasma bicarbonate level had risen to 16m Eq./1., but bicarbonate replacement on this day failed to keep pace with the huge losses, although the following day small positive balance was regained; nevertheless in this forty-eight hour period (Days 2 and 3, Diagram 1) she was in negative balance by 123 mEq., leaving a net positive balance for the first four days of treatment of only 77 mEq. In spite of this small increment, she felt and looked very much better, and her plasma bicarbonate concentration rose by Day 4 to 22 mEq./1. That this could happen in spite of such a small positive balance of bicarbonate is partly explained by the fact that she went into negative fluid balance on Days 1 and 2. During the first four days, the amount of sodium lactate she received was enough to cover her sodium requirements very precisely (Diagram 3), so that she stayed in sodium balance throughout. On Day 4 she was well enough to undergo an operation for repair of the fistula by which she was draining, and thereafter she made an uneventful recovery.

This case is an interesting, though extreme, example of the biochemical distortion which results from loss of large amounts of bicarbonate. The same picture may be seen, though in milder form, in patients with duodenal fistula and cases of ulcerative colitis, especially when they have ileostomies. Replacement with sodium chloride alone was sufficient to satisfy her sodium requirements and sustain the losses of chloride in the bile, but was useless in replacing bicarbonate which was being lost in the pancreatic secretion. Lactate is metabolized fairly slowly in the liver to bicarbonate and is safer for intravenous administration than sodium bicarbonate, the use of which needs to be controlled with frequent estimations of plasma bicarbonate to guard against the development of alkalosis.

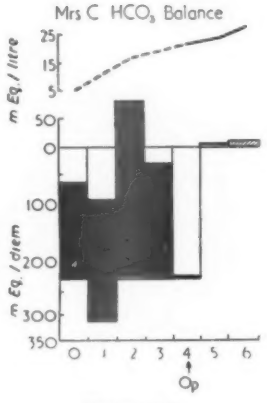

DIAGRAM 1.

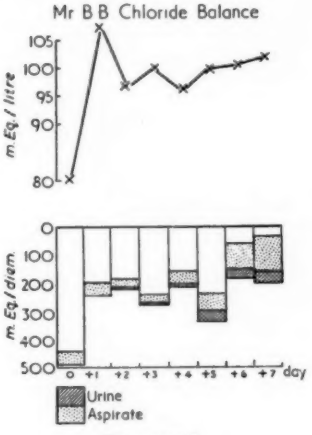

DIAGRAM 2.

Case II. Mr. B. B., aged 65. *Estimated body weight* 63·7 *kg.*

This patient was admitted with a history of vomiting for two months, due to pyloric stenosis from carcinoma of the stomach. He was clinically extremely dehydrated and almost comatose. His hæmoglobin concentration was 17·8 grams %, total plasma proteins 6·8 grams %, and his blood urea was 94 mg. %, laboratory evidence of hæmoconcentration. Plasma chlorides were 81 mEq./1., bicarbonate 40 mEq./1., and potassium 2·8 mEq./1., sodium 147 mEq./1. Therefore the biochemical distortion was one of hypochloræmic alkalosis and hypokalæmia, without depletion of sodium. In my experience this biochemical syndrome in cases of pyloric stenosis is less common than might be expected considering that loss of gastric acid is presumably an ineluctable part of the condition. There are three possible reasons for this: first, constant nausea may inhibit the secretion of free acid by the stomach, so that the loss of acid is not so great as might be supposed; second, the vomitus may contain large amounts of mucus which has a high sodium content, so that the loss of sodium parallels that of chloride, and the patient presents with what is in my experience more common, a mixed sodium and water depletion; third, these patients, and this applies especially to those with pyloric stenosis due to carcinoma, may not have a very high gastric acidity to start with.

The first necessity for treatment in this patient was to repair his chloride depletion, and with it as far as possible to correct the potassium depletion. Ideally one should give hydrogen ions with the chloride in such a case, since the alkalosis depends largely on loss of these in the gastric secretion rather than upon loss of chloride, and in this man's case there was no apparent depletion of sodium, although it is likely that the initial plasma sodium concentration was falsely high due to hæmoconcentration. Cooke and Crowley (1952) have described the use of a solution of ammonium chloride and potassium chloride for intravenous use. I have no experience of it, and had none at hand when this man was needing treatment, and in the event he received chloride in the form of sodium chloride. Where there is coexistent hypokalæmia, the administration of sodium chloride generally will only partly correct the alkalosis, final correction of which can only be made with potassium chloride.

I intended him to receive about 300 mEq. chloride in twenty-four hours, but the infusion was speeded up during the night, because he was not improving clinically, and by the end of the first twenty-four hours he had received 500 mEq. chloride (Diagram 2), the ratio of sodium to potassium being 10:1. This flooding with sodium might well have been catastrophic in an elderly patient, in whom the normal processes of osmotic adjustment are not brought into play so quickly as in the young; I have seen two men in their seventh decade who received only 350 to 400 mEq. sodium in a twenty-four-hour period, who both died with peripheral circulatory failure. However, this patient did not die, though his plasma sodium concentration increased to 170 mEq./l., and his plasma chloride to 107 mEq./l., while his bicarbonate dropped to 30 mEq./l. The fall in bicarbonate was only temporary, and due to the expansion of the extracellular fluid space, partially accommodating excess chloride and diluting bicarbonate. In this initial period he retained 3 litres of water. On Day 2 the bicarbonate was back at 39 mEq/l., and only became normal on Day 4, after which it remained normal.

The fact that the bicarbonate remained high during Days 3 and 4 was probably due to the fact that the potassium depletion had not yet been corrected.

Diagram 3 shows his potassium balance, and brings out one very important point, which is that in disease renal conservation of potassium is poor, in contrast to the state of affairs in the healthy subject (Fourman, 1952). During the first four days of replacement therapy the urinary loss of potassium equalled or exceeded the total input

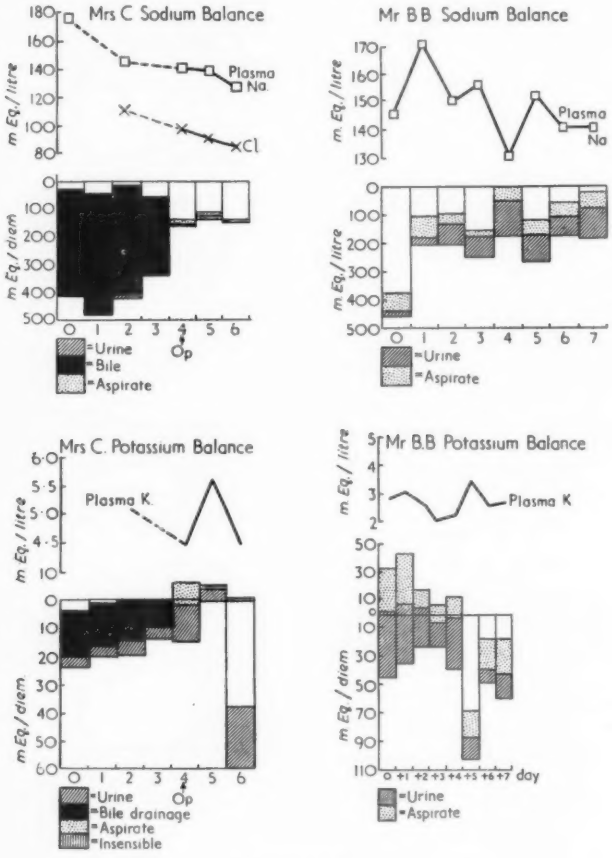

DIAGRAM 3.

by all routes, and it was only on the fifth day that he went into positive potassium balance. This coincided with the correction of his alkalosis. The total negative balance in the first four days was −103 mEq. which in considering his total depletion should be added to the almost certainly negative potassium balance which had been accruing during the two months during which he had been vomiting before admission. During the first six days in hospital the potassium concentration of the gastric aspirate varied from 35 mEq./l. to 15·5 mEq./l. which gives some idea of the magnitude of the loss from this source alone.

Renal loss of potassium is aggravated in patients receiving massive infusions of sodium and this is well illustrated by comparing the sodium and potassium balances of Case II with those of Case I (Diagram 3). During the first four days of treatment Case II was in strongly positive sodium balance, and his renal loss of potassium was high, while Case I was in precise sodium balance during the corresponding period of her illness, and her urinary potassium loss was only a fraction of her input and of her total loss, the bulk of which was in the fluid drained from the fistula. But her renal conservation of potassium was sufficiently good to ensure that she remained in potassium balance during that period.

The treatment of potassium depletion need not necessarily be by intravenous infusion when a patient is likely to return to oral feeding within four or five days. If intravenous potassium is necessary, any sodium and water depletion must be treated first to re-establish as far as possible proper renal function, since it is dangerous to give potassium when there is a high blood urea concentration and/or a poor urine output.

For intravenous administration of potassium I use 25 ml. of a 4% (w/v) aqueous solution of potassium chloride which is added to 500 ml. of 6% (w/v) dextrose, or 500 ml. of 0·18% (w/v) sodium chloride and 4% (w/v) dextrose solution. This provides 13 mEq. potassium in 500 ml. solution at a concentration of 26 mEq./l. It is remarkable how little potassium is needed to relieve the symptoms of deficiency and how much is necessary to repair a depletion completely.

The diagnosis of potassium depletion can often be made from the end of the bed. The patient's face is slack, expressionless and immobile, with eyes half-closed; he speaks in a whisper and may volunteer that he feels very tired; he may complain of pain in the legs and arms, but I have never seen a case of paralysis, even when the plasma potassium was as low as 1·5 mEq./l. I have found that the electrocardiogram so rarely shows the characteristic tracing (Howard and Carey, 1949) that it is useless in diagnosis. It is uncommon to see a patient with unequivocal symptoms whose plasma potassium is more than 3 mEq./l. and this may or may not be accompanied by alkalosis.

A depletion which resists repair for more than fourteen days carries a grave prognosis. I have seen two women, one with carcinoma of the cervix treated by Wertheim's hysterectomy, the other with carcinoma of the œsophagus treated by œsophagectomy, both of whom developed extensive sepsis after operation, and who became profoundly depleted of potassium. Although they received large amounts of potassium both orally and intravenously, their plasma potassium concentrations remained below 2·5 mEq./l. On the twenty-first day of the depletion they developed diuresis, but the blood urea levels rose at the same time. On the twenty-third day they went into noisy delirium, and on the twenty-fourth day they died. At autopsy the kidneys showed the signs of healed tubular necrosis. Another patient, also a woman, who had carcinoma of the cervix treated by anterior exenteration showed the same clinical picture after operation and the same renal findings at autopsy. The time relations in the development of symptoms were singularly constant.

Conclusion.—A knowledge of the mechanisms by which the body accommodates itself to depletion or repletion of its ionic constituents, forms an essential and vital part of understanding of nutrition in this field. The effects of deficiencies of ions, and of their replacement are often dramatic, and the possibilities of accurate replacement with modern laboratory aids are almost limitless provided always that one can anticipate the body's response.

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Dr. **Anne B. Sutherland**[1] (Edinburgh): I have heard with interest the papers given by Mr. Le Quesne and Dr. Merivale on the control of water and electrolyte balance, the abnormalities encountered and the methods employed for their correction. Mr. Brain has indicated that the problem of oral nutrition in terms of protein and calories is equally important. I would go even further and submit that complete nutritional care is a long-term policy extending beyond the immediate pre- and post-operative periods. The control of water and electrolyte balance is but the beginning of surgical convalescence after operation or injury. There is a general supposition that once intravenous therapy is discontinued the nutritional care of the patient becomes the responsibility of the nursing staff. This may be adequate for the short-term acute case, but there are few ward sisters in a busy surgical unit who can devote the time, or who have the necessary knowledge, to continue nutritional care satisfactorily into the later post-traumatic or post-operative phase. All too often a routine is adopted and is applied to every patient irrespective of his needs. Nutritional care is a form of therapy where each patient must be considered *as an individual.*

The question obviously arises as to whether or not specialized nutritional care is either important or necessary. I believe that in many cases it is. My own experience has been concerned mainly with

[1] In receipt of a grant from the Advisory Committee on Medical Research (Department of Health for Scotland).

cases of trauma and, more particularly, with burnt patients. While I realize that these form a separate group by the nature of their injury, they demonstrate general principles applicable to a much wider field. The following are some of the reasons why, in my opinion, continued nutritional care is important.

(1) It appears that it is possible to reduce the total amount of nitrogen loss and shorten the period of negative nitrogen balance and hence decrease the weight loss which accompanies it. I have not found that increased protein intake in this period merely increases the nitrogen excretion. As is known, it is not possible to eliminate the negative nitrogen phase, nor is it known if this be desirable. As Moore and Ball (1952) have stated, a transient nitrogen-negative period is not deleterious to the patient. Its prolongation by starvation may be fatal.

(2) In many cases weight-loss continues for a period far beyond that which can be explained by the nitrogen loss. This would appear to be due to no more than a caloric insufficiency. Further, when the caloric intake is inadequate the protein provided will be used, in part at least, to supply energy instead of to its much more important function of promoting tissue repair.

(3) In my experience the average patient's dietary intake in any surgical ward leaves much to be desired. I do not believe that this is an isolated finding confined to any one hospital. Even the hospital high protein diet, which I had assumed to be adequate, was shown by more detailed study not to be so. The *figures* given were, what the patient *actually consumed* was not. The prescribing of a high protein diet without knowledge of what it provides is to be condemned.

(4) Over a period of a month or longer an intake which may have been satisfactory in the first instance tends to become increasingly inadequate because:

(*a*) The nursing staff, perforce, no longer give the care and attention to feeding when the patient becomes one of the less seriously ill in the ward.

(*b*) The hospital diet tends to be monotonous.

(*c*) The appetite, so frequently a reflection of the general condition, is often so poor that those who need a high intake most are disinclined to eat.

(*d*) In any patient who requires frequent anæsthesia the *average* intake will be considerably lowered by the negligible amount consumed in each post-operative period.

OBSERVATIONS ON FOUR BURNT PATIENTS
33 DAY PERIOD

CASE	AGE	ADMISSION WEIGHT	PROTEIN INTAKE	PROTEIN INTAKE	CALORIE INTAKE	CALORIE INTAKE	DURATION OF WEIGHT LOSS	NUMBER OF ANAESTHETICS
	YEARS	KILOS	GRAMS PER DAY	GRAMS PER KILO PER DAY	PER DAY	PER KILO PER DAY	DAYS	
H. B.	40	57·7	65·0 —	1·1	1824 —	31·6	33	6
J.K.	29	67·8	136·0 *48·0*	2·0	3176 *972*	46·8	14	6
N.Mc	25	61·6	71·0 —	1·2	1956 —	31·7	19	4
S.Z.	27	62·0	103·0 *15·0*	1·7	3398 *1006*	55·0	0	4

FIG. 1.—The slanting figures refer to the amount of the total derived from the supplement.

To illustrate some of these points Fig. 1 is a brief summary of findings in 4 patients with burns. They form a reasonably comparable study from the point of view of their injuries; all had burns of the face, hands and forearms. They fell into two groups, however, as J. K. and H. B. required skin grafting of the hands, while N. Mc. and S. Z. did not. J. K. and S. Z. received an oral fluid supplement to the high protein diet of the hospital. The supplements were of two types, but both had a volume of 600 c.c. and provided about 1,000 calories. That given to J. K. had a higher protein content. Cases H. B. and N. Mc. received no supplement.

Cases J. K. and S. Z. were in one ward, H. B. and N. Mc. in another.

The main points to note are:

(1) The difference in the ward protein intake in the two wards—88 grams in one, and 65 to 71 grams in the other. The only explanation which can be offered for this is the different attitude towards nutritional care of the ward sisters concerned.

(2) In such patients as these the levels of intake should probably be 1·5 to 2 grams of protein and 45 calories per kg. body-weight. It will be seen that *total* figures of protein and calories can be mis-

leading: 71 grams protein and 1,956 calories might seem to be a reasonable intake, whereas, when related to intake per kg. only those receiving the supplement reached the desired levels.

(3) There is variation in weight-loss.

(*a*) Case S. Z. showed no weight-loss and in this patient the negative nitrogen phase was of very short duration, despite the fact that the supplement provided little extra protein. Was it then that the protein given was available because of the sufficiency of calories from other sources, and that the caloric intake was adequate for weight to be maintained?

(*b*) Similarly, was the much shorter duration of weight-loss in J. K., as opposed to that in H. B., due to his receiving an adequate caloric intake rather than to his extra protein intake?

(*c*) There is little doubt that the low intakes in H. B. and N. Mc. following anæsthesia did much to bring down their average intakes, whereas in J. K. and S. Z. the supplements were acceptable and well tolerated in the post-anæsthetic period and did much to maintain average intakes at a higher level.

Any form of therapy which will hasten recovery and shorten the duration of hospital stay is important. I believe that adequate nutrition is such a form of therapy.

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[*April* 30, 1954]

MEETING AT GUY'S HOSPITAL, LONDON, S.E.1

A Note on the Anatomy of the Anal Canal

By A. G. PARKS, M.Ch., F.R.C.S.

IN view of the many conflicting opinions which have been expressed in the last hundred years on the anatomy of the anal canal [1–6], I have made another study of the problem. This investigation has been limited to the superficial tissues of the region, no attempt has been made to examine the deeper parts of the external sphincter, or the levator ani.

Milligan, Morgan *et al.* [5, 6] described a depression occurring between the internal and external hæmorrhoidal plexuses which is apparent on clinical examination or at operation. The depression is found at the mucocutaneous junction where stratified squamous epithelium changes to stratified transitional epithelium; this is the line of the anal crypts. They ascribed the depression to the attachment of the longitudinal muscle of the rectum to the mucocutaneous junction and called this the anal intermuscular septum because it passed between the internal and subcutaneous external sphincters. It was said to divide the space between epithelium and muscle into two portions; the upper or submucous space contained the internal hæmorrhoidal plexus, the lower or perianal space contained the external hæmorrhoidal plexus. The perianal space was bounded medially by the anal intermuscular septum and laterally was continuous with the ischiorectal fossa.

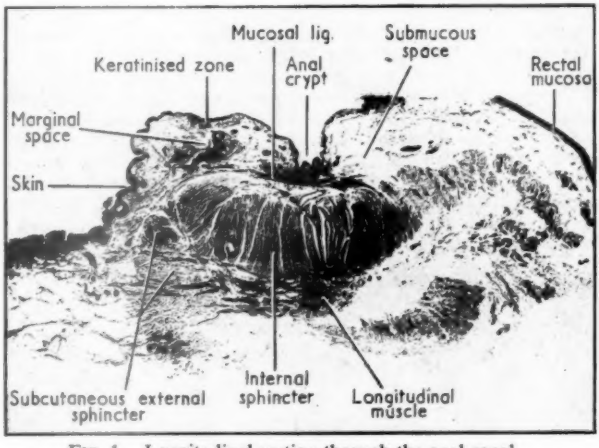

FIG. 1.—Longitudinal section through the anal canal.

Academic anatomists have described neither the inter-hæmorrhoidal groove nor the anal inter-muscular septum. The groove is not visible in preserved tissue because the veins of both hæmorrhoidal plexuses are empty. In order to study this region in a state resembling the living, I have injected the submucosa and subcutaneous tissues of specimens with saline before fixing them in formalin. This distends the submucosal space and renders the inter-hæmorrhoidal depression readily apparent. Longitudinal sections were then made by routine histological techniques.

The results of this investigation are shown in the photograph of one of the specimens (Fig. 1) and in the illustration (Fig. 2) which is a diagrammatic representation of the anatomy found in all the specimens. Milligan, Morgan *et al.* described the subcutaneous external sphincter as forming the lower one-third of the muscular wall of the anal canal. The present study confirms the views of the academic anatomists who have shown that the internal sphincter forms the entire muscle wall of the canal. I have also verified this clinically at operation by biopsy of the muscle ring which presents at the anal margin. On 8 out of 9 occasions the section has shown the tissue to be smooth muscle of the internal sphincter.

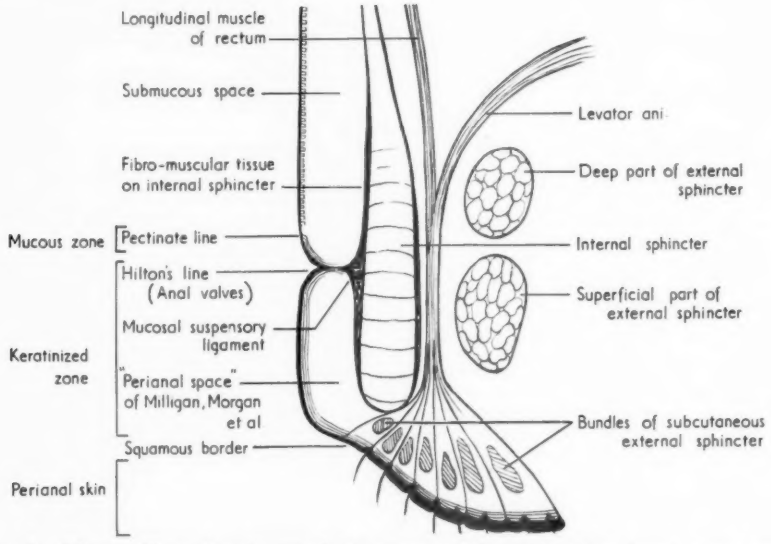

FIG. 2.—Diagram illustrating the superficial anatomy of the anal canal as found in specimens studied by the author. The perianal space has been re-named "the marginal space."

The groove or depression between the hæmorrhoidal plexuses is seen to be caused by fibrous tissue from the sheath of the internal sphincter passing out to be inserted into the mucosa of the anal crypts. I have called this fibrous tissue band the mucosal suspensory ligament. It forms the upper and medial boundary of the space which Milligan, Morgan *et al.* termed perianal but which I prefer to call marginal, because part of it is found within the anal canal. The marginal space, containing the external hæmorrhoidal plexus, is bounded laterally by the insertion of the longitudinal muscle into the perianal skin. This description explains the clinical observation that perianal abscesses and hæmatomata do not spread into the ischiorectal fossa as we should expect were the views of Milligan, Morgan *et al.* [5, 6] correct.

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Section of Urology

President—HUGH DONOVAN, M.B., F.R.C.S., F.R.C.S.Ed.

[*May* 27, 1954]

DISCUSSION ON THE SURGERY OF THE ADRENAL CORTEX

Dr. A. C. Crooke: The supply of cortisone is now sufficient to allow major surgery of the adrenal glands to be carried out on an increasing scale. Partial resection or complete ablation of the glands is practised in a number of centres for three apparently unrelated conditions, namely, certain types of Cushing's syndrome, of hypertension, and of cancer.

When Cushing's syndrome is associated with a tumour of the adrenal cortex, thymus, ovary or pancreas the removal of the tumour is the first consideration, but in the absence of such a tumour treatment aims at lowering circulating corticoids from pathologically high to normal levels. The most rational method of achieving this is by surgery (Priestley *et al.*, 1951; Sprague, 1953) but it is debatable whether total adrenalectomy and subsequent maintenance with cortisone, or subtotal adrenalectomy, is better treatment. We believe that the latter is better but it is technically difficult for the surgeon to decide how much cortex to retain. With experience we think it should generally be possible to conserve an amount of cortex which is just sufficient for the patient's needs, leaving her independent of cortisone therapy. We feel convinced that total adrenalectomy is no more justified for Cushing's syndrome than is total thyroidectomy for Graves' disease.

Mr. Hugh Donovan has now performed subtotal adrenalectomy on 5 patients who have been followed for at least eight months after the operation.

This series is too small to draw any firm conclusions but we have observed repeatedly a fall in the level of circulating corticoids from very high to normal which has coincided with the disappearance of symptoms of Cushing's syndrome. We have been impressed with the reduction in the blood pressure in 2 patients from a level of around 240/140 mm.Hg, which had persisted for over a year in each case, to around 120/80 mm.Hg. 2 patients died. One had gross arteriosclerosis and hypertension, and had had two strokes before operation, and the other had severe mental changes. We are inclined to agree, therefore, with workers at the Mayo Clinic who regard severe arteriosclerosis and gross mental changes as contraindications to surgery.

We do not think that the treatment of the adrenogenital syndrome with adrenocortical hyperplasia should be surgical. Medical treatment with cortisone offers greater promise and was discussed by Dr. Lawson Wilkins at the meeting of the Section of Endocrinology held on May 26, 1954 (*See* Wilkins, 1955).

Hypertension is but a symptom of several diseases and adrenalectomy has been carried out somewhat indiscriminately for a number of these by different groups of workers. Jeffers *et al.* (1953) have described their results on a series of 99 patients. About half of them improved but most had also had some form of sympathectomy which makes it difficult to assess the value of adrenalectomy in these patients. Pickering *et al.* (1952) were able to show by histological examination of the kidney that adrenalectomy could reverse the characteristic changes of malignant hypertension. We have also seen the blood pressure of a woman which was consistently above 220/120 mm.Hg restored to normal after adrenalectomy despite the fact that histological examination of a biopsy specimen of the kidney showed the classical picture of malignant hypertension. This patient is now free of symptoms on a daily dosage of 50 mg. cortisone. We have also seen another woman whose diastolic blood pressure was unaffected by surgery. It remained at 140 mm.Hg despite the fact that she was kept for several days on the verge of adrenal crisis which lowered the systolic pressure until the pulse pressure was only 10 mm.Hg. Six weeks after the operation she had a cerebral hæmorrhage and died. The difference between these 2 patients lay mainly in the fact that arteriosclerosis was gross in the latter and relatively much less severe in the former. These results are remarkably similar to those which we obtained in our series of patients with Cushing's syndrome and add weight to our observation that severe arteriosclerosis is a contraindication to surgery, but we believe that adrenalectomy offers the prospect of relief in certain carefully selected patients with essential hypertension.

It is not clear why adrenalectomy and subsequent maintenance with cortisone should restore the blood pressure to normal. It may act by lowering the overall level of circulating corticoids or by preventing the rise in the level which accompanies stress or, more likely, it may remove some undesirable corticoid from the circulation which is then replaced by less noxious cortisone.

Cancer.—It has long been known that certain cancers of the breast and prostate are influenced by gonadectomy. It is recognized that the responsible factor is the level of the circulating sex hormones. This effect can also be achieved by giving hormones of the opposite sex, like stilbœstrol for cancer of the prostate and testosterone for cancer of the breast. Unfortunately a small proportion of the sex steroids is derived from the adrenal cortex and this amount is increased after gonadectomy. Adrenalectomy has therefore been performed to remove this source of sex hormones. After surgery patients require cortisone, a small proportion of which is converted into sex steroids. Birke and Plantin

(1954) have shown that between 1% and 2% of the cortisone and between 1·5% and 8% of compound F, or cortisol, is excreted as 17-ketosteroids. It seems, therefore, to be impossible to abolish the excretion of all 17-ketosteroids from urine, and the same probably applies to œstrogens. Nevertheless, this further reduction in the level of excretion of sex steroids by adrenalectomy has apparently benefited a proportion of the patients with cancer of the prostate or breast, and this form of treatment is now being used in a number of centres.

It is perhaps not widely enough known that cortisone inhibits the secretion of ACTH by the pituitary gland and that in doses of about 50 mg. daily it causes severe atrophy of the adrenal cortex. This depresses the production of sex steroids by the cortex and the level of 17-ketosteroids falls to about the same extent as that which obtains after adrenalectomy (Birke *et al.*, 1954). A number of workers have made use of this observation in the treatment of patients with cancer and have claimed considerable improvement (Harrison *et al.*, 1952; Thompson, 1952; Birke *et al.*, 1954).

It is questionable whether adrenalectomy for cancer can be regarded as an ethical procedure until it has been shown beyond all doubt that a couple of pills of cortisone a day taken by mouth will not achieve the same result—pills which the patient would have to take anyhow.

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Mr. D. Innes Williams: My contribution is concerned with a group of cases which may be included under the term *the adreno-genital syndrome.*

We are concerned then with hyperplasia of the adrenal cortex and with tumours producing genital changes. The hyperplasias are frequently congenital and their effects are evident at birth; but an onset in later life is also seen. Pathologically the condition is a hyperplasia rather than a simple hypertrophy, and we are dealing with something much more complicated than a gland producing an excessive quantity of its normal secretion. The cells constituting the hyperplastic gland resemble most nearly those of the zona reticularis of the normal cortex, but this layer is not normally distinguishable in neonates. The girls affected by the condition have usually such virilizing changes at birth that they fall into the category of pseudohermaphrodites and are not infrequently regarded as boys. The deviation from normal development appears to have taken place after the full differentiation of the uterus, tubes and ovaries, but the later descent of the vagina and opening out of the urogenital sinus is prevented, so that at birth the vagina opens into the urethra at approximately the level of the perineal membrane. At the same time closure of the urethral folds is induced with hypertrophy of the phallus, and the clitoris therefore takes on the appearance of a penis, with some degree of hypospadias. The labio-scrotal folds may also unite to form an empty scrotum. The virilizing effect of the excessive androgen secretion does not cease at birth and progressive masculinization is evident. The clitoris continues to enlarge, so that a girl of 4 or 5 may have what is almost the equivalent of an adult-sized penis. Pubic hair appears early and the face is frequently disfigured by pimples and greasy skin which might be anticipated in an adolescent boy. Somatic growth is considerably accelerated, centres of ossification appear early and fusion of the epiphyses is also premature. Thus, although in childhood sufferers from this condition are considerably larger than their contemporaries, ultimately their growth is stunted and they do not attain average adult proportions. The masculinization may affect the psychology as well as the physique, and this condition is not infrequently accompanied by a troublesome behaviour disorder. Menstruation and breast development do not occur at puberty. In the boys with adrenal hyperplasia there is the same acceleration of somatic growth and an isosexual precocity. They are sometimes said to exhibit precocious puberty; it is not the testicles themselves which develop, but the androgenic stimulation of the secondary sexual characteristics gives the appearance of puberty. The increased androgen secretion in both sexes is reflected in the increased excretion of urinary 17-ketosteroids, and this fact provides a useful laboratory check on the progress of the disease. The normal ketosteroid excretion of a newborn baby is less than 1 mg./twenty-four hours, and even at birth the babies with adrenal hyperplasia frequently excrete as much as 5 mg./twenty-four hours. Progressively larger amounts are encountered with increasing age, so that at the age of 6 or 7 years it is not uncommon to find 50 mg./twenty-four hours.

So far we have noted only the effects of over-activity on the part of the adrenal gland, but during their infant years both males and females suffer a much more complicated biochemical disturbance, due perhaps to a deficiency in the secretion of the electrolyte-regulating hormones of the adrenal cortex or perhaps to the secretion of an unusual type of steroid hormone. Thus these infants suffer from vomiting and dehydration, the symptoms often appearing during the first weeks of life and

sometimes mistakenly attributed to pyloric stenosis. Crises occur which in some ways resemble the Addisonian crises of cortical deficiency states in adult life. Investigations during these episodes show a lowered serum sodium and chloride level with a considerable rise in the serum potassium. Such crises have been responsible for a considerable mortality in this group, and they may come with surprising suddenness in an apparently healthy child.

The effects of cortisone administration.—It has been the finding of all observers that the administration of ACTH has no effect except to lead to a slight increase in ketosteroid excretion. Cortisone, on the other hand, produces a striking change. The output of ketosteroids rapidly drops to a normal level if the dosage is properly adjusted; the biochemical changes, i.e. the raised potassium and lowered sodium levels, are corrected much more promptly and more effectively than is possible by the use of DOCA, and in the long run cortisone brings to a halt or reverses the virilizing trend in older children and adolescents. It has been shown to allow the development of breast tissue and the commencement of menstrual periods. It cannot, of course, lead to any change in the established anatomy of the pseudohermaphrodites, nor does it seem to shrink the enormously hypertrophied clitoris. One curious feature is that a few of the children suffering from a severe behaviour disorder show an improvement while they are on cortisone. The effects of this drug last only so long as it is administered, and all the previous changes recur if the cortisone is withdrawn. It appears in fact to be replacement therapy, similar, though on a rather different time scale, to the administration of insulin in diabetes. It is very plausibly suggested that these adrenal glands are unable to carry out the normal synthesis of compound F, the appropriate steroids being diverted into the production of androgens. The deficiency of compound F in the circulation stimulates the output of ACTH which brings about adrenal hypertrophy, so that the production of the electrolyte-regulating hormones is brought up to normal, but only at the expense of an enormous over-production of androgens. In this connexion, I may mention that an analysis of extracts of an adrenal from one of these cases, performed by Miss C. E. de Courcy at The Hospital for Sick Children, showed an absence of corticosteroids, but the presence of a considerable quantity of pregnanetriol, a substance derived from one of the precursors of compound F. No obvious change in the pathology of the glands results from the administration of cortisone so far as we have been able to determine; in the long run one might expect that the functional "suppression" would be followed by diminution in size.

Coming then to treatment, it will be clear that we have already a considerable bias in favour of the administration of cortisone rather than the surgical removal of the hypertrophied adrenals. In the babies, the danger to life is from the electrolyte disturbance and the Addisonian crises, and in view of the rapid improvement on cortisone, I think one would have to be a brave surgeon to undertake adrenalectomy at this stage. Later on we must consider the sexes separately: in boys the serious development which we wish to avoid is the dwarfism resulting from premature fusion of the epiphyses. We are not at present in a position to say that cortisone will achieve this end, but if we are to judge the restitution of normal balance by the excretion of 17-ketosteroids, there can be no doubt that cortisone is more effective than unilateral adrenalectomy and probably more effective than subtotal adrenalectomy, and we should therefore expect to obtain more normal conditions for bony development by cortisone administration. It would scarcely be justifiable to undertake total adrenalectomy for a condition such as this, which does not involve in the later stages any danger to life. Cortisone should not be necessary once growth is complete. In the females we encounter two distinct groups. In one, the child has always been regarded as a boy and regards herself as a boy, and in later life is quite content to assume the male role in sexual relations. In such a case one is rather reluctant to give any treatment at all, since the cure of the condition must involve a change in the accepted sexual role and lead to very serious psychological complications which the results can scarcely justify. Where the child has been regarded as a girl, on the other hand, the reversal of the virilizing changes is unquestionably indicated, and cortisone should certainly be administered, even though it means treatment continued indefinitely. It is very doubtful whether menstruation will be established after unilateral adrenalectomy but this operation might be considered if severe cortisone side-effects were encountered.

My own experience of this disease comprises 12 cases, 11 of them female and one male, seen in consultation with medical colleagues at The Hospital for Sick Children and elsewhere. 7 of the females and the male have been treated by cortisone at one time or another. 2 of the female pseudohermaphrodites were well-developed boys in appearance and in the eyes of their parents, and no treatment was advised, the parents being given to understand that a degree of dwarfism must be expected. 2 of the girls had only a very mild degree of the condition, with hypertrophy of the clitoris as the chief sign, and they are still being watched without treatment. 2 cases have died with a severe and sudden biochemical storm; although in one of these cortisone had been regularly administered with apparently satisfactory effects. This latter was, of course, a great disappointment to us, and is still rather a puzzle.

Adrenal cortical tumours as a cause of the adrenogenital syndrome.—Tumours may be adenomata or carcinomata, but the distinction is not always easy, and even well-encapsulated growths may be histological high-grade carcinoma. Cortical tumours are usually virilizing in females of any age, and they cause iso-sexual precocity in male children. A clear-cut separation of those causing Cushing's syndrome is not always possible, and the effects are often mixed. On rare occasions the tumours have a feminizing effect in adult men and one similar case is recorded in a boy. Others produce no obvious

endocrine disturbance and are brought to the attention simply by the presence of a lump or of metastases.

The differentiation of adrenal tumour from adrenal hypertrophy is of some importance, as in the former case there may be no obvious sign of the lump. A late onset will naturally favour tumour, though it is not diagnostic: abnormalities of fœtal development will naturally indicate congenital hyperplasia. In both the 17-ketosteroids will be high, but much higher figures are reached in the tumour cases; moreover with the tumours it is not possible to reduce to normal the ketosteroid output by the administration of cortisone, though slight and temporary reductions may be achieved.

Mr. L. N. Pyrah: *Bilateral Adrenalectomy in the Treatment of Mammary and Prostatic Cancer.*

Any measures which are claimed to benefit advanced malignant disease must be examined critically and their value assessed. Because of the recent work of Charles Huggins and his co-workers (Huggins and Bergenstal, 1951*a*, *b*; 1952*a*, *b*; Huggins and Dao, 1953) interest has lately centred upon the treatment of mammary and prostatic cancer by bilateral adrenalectomy.

It has been known for many years that some cancers in these situations can be influenced by the hormones of the host, both in man and in animals; such neoplasms may be called dependent or conditioned. The cells of such neoplasms may, however, change their character, cease to be controlled by hormones and become autonomous. Huggins and Bergenstal (1951 *a*, *b*; 1952 *a*, *b*) thought that in the case of some cancers of the breast and of the prostate in which there had been a regression of the growth following hormone deprivation or therapy and in which there had then been a relapse, there may have been a further build-up of a cancer-controlling substance within the adrenal glands. These workers have reported bilateral adrenalectomy in 55 cases of breast cancer (Huggins and Dao, 1953) and in 7 cases of prostatic cancer (Huggins and Bergenstal, 1952 *a*, *b*), and have shown by clinical, radiological and histological studies that a regression of cancer occurs in some cases.

I will first briefly review some of the known facts concerning the relationship between gonadal hormones and breast and prostatic cancer in animals and in man.

Carcinoma of the Breast and the Gonads

(1)—*In mice.*—Lathrop and Loeb (1916), using female mice of different strains (some having a higher incidence of spontaneous mammary cancer than others), found that oophorectomy reduced the incidence of breast cancer but did not entirely prevent it. In cases in which cancer developed, it did so at a later age in the oophorectomized mice.

Other workers (Lacassagne, 1932) injected œstrin into young mice belonging to a strain the males of which were not affected by cancer but the females showed a high incidence of spontaneous mammary cancer. Cancer of the breast developed within six months in the 3 male mice so treated and in 1 of the 2 females.

Bonser (1936) injected œstrone into male mice of a high cancer strain of which normally the females alone developed cancer. The breast showed proliferation of the acini and dilatation of the ducts; 3 out of 23 mice so injected developed mammary cancer.

Fekete and his co-workers (1941) found that in spayed mice considerable amounts of œstrogen were produced during later life probably from the adrenals; these glands underwent hypertrophy and yellowish nodules were found in the cortex. Gardner (1941) found that adrenal tumours developed in 13 of 15 spayed mice aged 43 to 65 days; there was, in addition, evidence of pronounced œstrogenic activity such as changes in the vaginal and uterine epithelium.

(2) *In man.*—Sir George Beatson of Glasgow (1896) was the first surgeon to record clinical improvement in 2 of 3 cases of advanced breast cancer in which he had performed oophorectomy. Lett (1905) reported improvement in 23% of 99 collected patients with advanced breast cancer, for whom oophorectomy had been performed. In the male, Treves (1949) reported a remission following orchidectomy in 3 of 6 cases of male breast cancer having metastases; there was recalcification of bone metastases and relief of pain.

Irradiation of the ovaries as an alternative to oophorectomy was first used by de Courmelles (1922), and regressions of the metastases lasting up to three years have been reported by some workers.

In order to neutralize œstrogen, testosterone was first used by Loeser (1938 *a*, *b*) for cases of inoperable or metastasizing breast cancer, with benefit in some cases. Synthetic œstrogens (stilbœstrol and dienœstrol), have also been used for treatment; Haddow and his co-workers (1944) reported improvement in 26·5% of 204 patients treated by œstrogens for periods of one to nine months. Relapse eventually took place.

Cancer of the Prostate and the Testes

It was shown by Huggins and Clark (1940) that spontaneous enlargement of the prostate in senile dogs underwent regression following castration or after the administration of œstrogen. This work suggested that in those malignant tumours of the prostate in man in which there was a preponderance of mature epithelium there might be a favourable response to anti-androgenic procedures. The synthesis of stilbœstrol by Dodds and his co-workers (1938) provided a readily available œstrogenic substance of great activity which could be administered by mouth. Huggins and Hodges (1941) showed that in some cases of prostatic carcinoma with bone metastases castration (or partial deprivation of androgen), or alternatively the administration of œstrogen resulting in a partial suppression

of androgen, resulted in some cases in a clinical remission of the growth with disappearance of bone metastases. The administration of androgens on the other hand caused an activation of the tumour. In cases which respond, after a varying interval of time the period of regression terminates apparently because of the synthesis of gonadal hormones elsewhere and "mainly because of the functional metaplasia of cells of the adrenal cortex" (Furth, 1953).

Scott and Vermeulen (1942) showed that after a time orchidectomy in males suffering from prostatic cancer is usually followed by an increase in 17-ketosteroids in the urine. Huggins and Scott (1945) showed that these high values are eliminated by bilateral adrenalectomy and thereafter only small amounts of 17-ketosteroids are found in the urine.

Present Series

The series which I am reporting consists of 28 cases which have had bilateral adrenalectomy between April 1953 and April 1954, 25 being cases of carcinoma of the breast and 3 carcinoma of the prostate. All the breast cases had widespread metastases with or without previous mastectomy; the prostate cases had metastases and had had previous perurethral resection. Although Huggins had shown that a favourable response after adrenalectomy occurred in the more highly differentiated growths of the breast or the prostate, namely those which had an alveolar or papillary adenocarcinomatous structure on microscopic examination, it was decided to operate on all cases referred, providing it was thought they had a fair chance of withstanding the operation. Most of the cases were ill, some had been bedridden for some weeks. When the patient was reasonably fit adrenalectomy and gonadectomy were performed at the same operation; in the earlier cases in the series and in those who were gravely ill, the second adrenal was removed at a second operation a fortnight after the first.

Substitution therapy.—The substitution therapy suggested by Huggins and Bergenstal (1951*a*, *b*) has been used and has been proved satisfactory. Without the use of cortisone the patient would die. On the day before operation 50 mg. of cortisone was given six-hourly and also 3 mg. of deoxycortone acetate (DOCA). On the day of the operation a bigger dose of cortisone is required; 150 mg. was given one hour before operation and 50 mg. four-hourly post-operatively, the dose being reduced to six-hourly on the first post-operative day and twelve-hourly for the four succeeding days; 5 mg. of DOCA, reduced to 3 mg. on the first and succeeding post-operative days, was also given as a corrective against salt loss. It was possible in nearly every case to achieve a permanent maintenance dose by the sixth post-operative day of 25 mg. of cortisone by mouth twice daily and 0·3 mg. of DOCA intramuscularly. When the patient was convalescent, 300 mg. of DOCA in the form of pellets was implanted subcutaneously; this has to be repeated once every six months. Sodium chloride in capsules has been given by mouth (3 grams per day) beginning on the day before operation.

The adrenals were removed using intravenous thiopentone to induce anæsthesia, followed by intratracheal gas and oxygen. Tubocurarine was given as a relaxant. The blood pressure was carefully watched and noradrenaline was kept in readiness to be given through an intravenous drip in case of hypotension, but it did not, in fact, have to be used.

Operative technique

Adrenalectomy.—The adrenals were removed through two separate incisions in the loins, the patient being placed on her side. An incision was made over the twelfth rib and carried forward obliquely as for exposure of the kidney. The upper pole of the kidney was mobilized and held downwards by the fingers and at this stage the adrenal gland became visible and was easily recognized by its bright yellow colour. The gland is rather friable so that retractors must only be applied to the surrounding fibrous tissue and not to the gland itself, and only then with caution. Dissection is carried out partly with blunt scissors and partly by the index finger. On the right side, the gland is freed from the posterior surface of the liver and its deep surface is dissected away from the inferior vena cava upon which it lies; it is attached to this by the short, stout adrenal vein which is accompanied by the adrenal artery. The gland is dissected out on its free and its deep surfaces, and is left attached to the pedicle which is ligatured last, the gland then being cut away. The left adrenal gland is of a different shape and its lower pole lies in close relation to the left renal vein which requires to be demonstrated to guard against injury. Once this is done, there is no difficulty in securing the rather long pedicle.

An important finding was that both adrenal glands were found infiltrated with cancer in 10 cases. Under such circumstances, the gland is enlarged and is firmer in texture than the normal gland. Unless the enlargement is very advanced involvement in cancer does not render the surgical removal much more difficult.

Gonadectomy.—The ovaries were removed through a lower abdominal midline incision and the testes were eviscerated through a midline scrotal incision if they had not been previously removed.

Post-operative course.—The majority of patients stood the operation well, even though they often appeared to be very feeble. A considerable reduction of blood pressure occurred in 5 cases and its prolongation in one very ill patient was responsible for a post-operative fatality. In cases which had a major regression the patient experienced a sense of well-being soon after the operation and pain disappeared within forty-eight hours. Even when there was not much regression of growth, the feeling of well-being was still noticeable and pain was very often relieved. The cortisone and the DOCA in the doses recommended took care of the maintenance of the electrolytes and there was no real worry about excessive loss of salt. Patients were got out of bed when possible within two or three days of

the operation, unless extensive bone metastases indicated caution to prevent fracture of bones which were the seat of metastases.

Results

Carcinoma breast

Cases improved:
- Major remission, patients alive and well .. 4
- Major remission followed by relapse and death 5
- Moderate improvement, probable remission .. 1

Cases unimproved:
- Died of cancer without clinical improvement .. 8
- Alive but not showing improvement 4
- Post-operative deaths 2

Too early for assessment:
- Alive and well 1

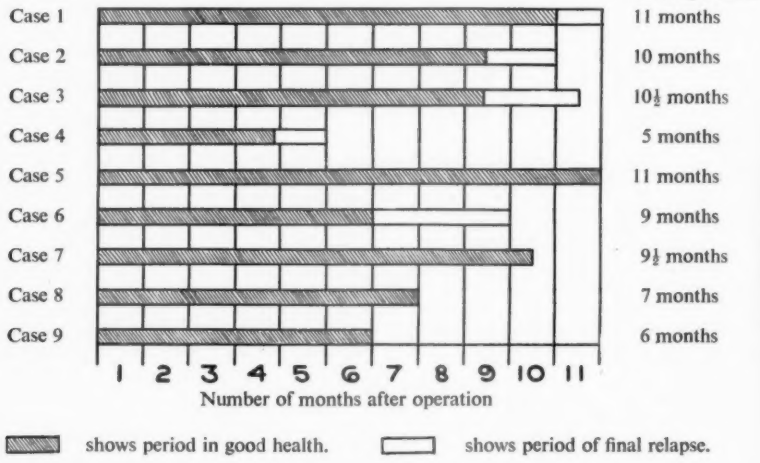
25

Carcinoma prostate
- Clinical improvement followed by relapse and death 2
- Died of cancer without clinical improvement .. 1

3

It is seen that several major remissions have occurred with the breast cases, but none with the prostate cases; 3 cases, however, is too small a series upon which to base an opinion. Fig. 1 gives details of the survival of those cases in which a major remission occurred.

Fig. 1.—9 Cases with Major Remission



Detailed case histories with radiographs and histological sections of some of the cases having major remissions have been reported elsewhere and the reader is referred to this paper (Pyrah and Smiddy, 1954); only one case will be recorded here which showed a major remission.

Case Report

V. D., female, aged 36 years. The patient had a right radical mastectomy in 1948 for spheroidal cell carcinoma. In 1952 she had massive recurrence in the spine and pelvis causing pain. On examination, 1.8.53, she was bedridden and emaciated; she complained of pain in the spine, the right leg and right hip. There was an ulcerated sacral bedsore and lymphœdema of the right arm from the elbow downwards. Radiography demonstrated gross osteolytic secondary deposits in the ribs, dorsal and lumbar spine, the pelvis, both femora and both tibiæ (Figs. 2 and 3).

Operation (7.8.53).—Bilateral adrenalectomy and oophorectomy (one-stage).

Result.—From the fourth post-operative day she had major relief of pain. Radiological improvement of the bone secondaries was slow. At first, owing to the extreme decalcification she was kept in bed for fear of a spontaneous fracture. Her health gradually improved, the bedsore healed, and the right arm improved. Improvement after the first six weeks was fairly rapid. The radiographs (Figs. 2 and 3) show the extent of the recalcification of the femur and of the pelvis. She is now fully mobile, fit and well, she has put on 5 st. in weight, and is doing her housework. This is a major remission after 288 days.

Discussion

Mammary carcinoma.—Huggins and Dao (1953) reported 55 cases of breast cancer treated by bilateral adrenalectomy with or without gonadectomy during 1951 and 1952 (2 men and 53 women). 3 women died within thirty days of the operation. 20 cases had had a remission of varying magnitude, patients having osseus and pleural metastases showing the best results.

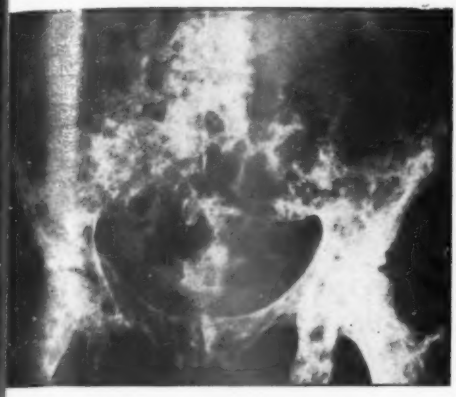


FIG. 2.—(A) 26.6.53 (before operation): Bone metastases in pelvis, vertebræ and upper ends of both femora.

FIG. 2.—(B) 15.4.54: Pelvis thirty-five weeks after operation.

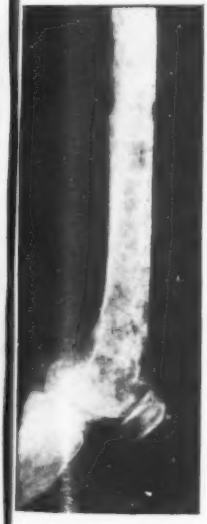


FIG. 3.—(A) 25.7.53: Left femur before operation.

FIG. 3.—(B) 14.10.53: Left femur ten weeks after operation.

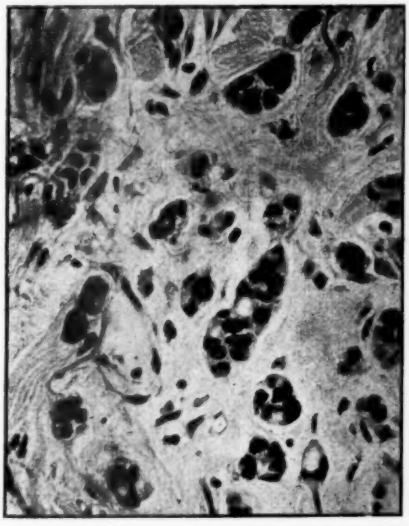


FIG. 4.—Skin nodule from breast cancer. This shows the typical alveolar structure regarded as favourable for adrenalectomy. This patient had a major regression lasting for eight months after operation.

Pearson *et al.* (1953) reported remissions in 5 of 12 cases of advanced mammary cancer submitted to bilateral oophorectomy and adrenalectomy.

The findings in this series confirm the work of Huggins and his co-workers that a major remission can be achieved in some patients with advanced mammary cancer by bilateral adrenalectomy and oophorectomy. A little more than a third of all the patients treated achieved an objective remission and this proportion is probably exceeded in the cases of breast cancer. In the cases that have responded there has been a great improvement in general health, and radiographic follow-up has demonstrated regression of bony and thoracic metastases (Pyrah and Smiddy, 1954). It seems likely that metastases in the liver and in the abdomen also regress. The longest case in this series is alive and well ten months after operation. The cases which have responded best (Fig. 4) have had a growth which had an alveolar or a papillary or an adenomatous structure; in other words a highly differentiated cancer. In one patient two different types of histological pattern were shown to exist in different metastases,

so it is not always wise to rely on a single biopsy when deciding for or against adrenalectomy. In one patient the sole report obtained so far has been that of spheroidal cell carcinoma.

The mode of disappearance of the visible growth in the breast or the skin nodules, has been a gradual shrinkage. Fig. 5 shows the fibrosis in a skin nodule which is obtained after a response. Whether

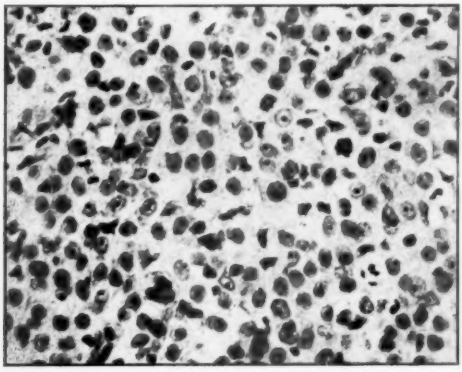


FIG. 5.—(A) Skin nodule before adrenalectomy showing spheroidal cell carcinoma.

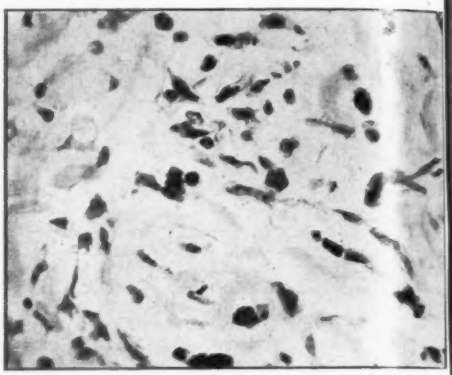


FIG. 5.—(B) Skin nodule two months after operation showing fibrosis and degenerate cancer cells.

the cells that remain are degenerate or whether they are still visible, it is impossible to say. In some of my cases the cancer has regressed on the chest wall but advanced elsewhere, for instance in the abdomen, to a fatal issue. Pearson *et al.* (1953) reported similar cases.

As to whether hypertrophy of accessory cortical adrenal tissue is responsible for relapse after a major regression is doubtful. Graham (1953) reported accessory adrenal tissue in 32% of autopsies, the average size of the gland being $7 \times 4 \times 3$ mm. This would appear to be too small to be responsible for the relapse; no case, so far as I am aware, has been reported in which cortisone has been withdrawn in an adrenalectomized patient, who has been able to survive because of the existence of accessory cortical tissue.

The pituitary gland has been removed for metastases in breast cancer by Luft and Olivecrona (1953). If the pituitary hormones stimulate the production of œstrogens in the adrenal this would appear theoretically to be a reasonable procedure. One successful case was reported. It seems, however, to be difficult to be certain whether the whole of the pituitary tissue can be removed at operation, and if this is not done, no regression of the cancer can be expected.

Prostatic carcinoma.—Huggins and Bergenstal (1952*a*, *b*) recorded the results of bilateral adrenalectomy in 7 patients suffering from prostatic cancer. There was one post-operative death and a second patient died from acute pulmonary œdema forty-nine days after operation. 3 patients had clinical remissions of considerable magnitude and were alive respectively 240, 158 and 180 days after operation.

Scardino *et al.* (1953) reported 3 cases of prostatic cancer treated by bilateral adrenalectomy. One case is free from symptoms nine months after operation; a second survived four months dying from cardiac failure; the third died from carcinomatosis four months after operation having shown no improvement.

The 3 cases of prostatic cancer reported in the present series are inadequate to form an opinion as to the efficiency of the treatment. There was, however, some clinical improvement in 2 of the 3 cases treated.

CONCLUSION

The results of bilateral adrenalectomy as a treatment for advanced mammary and prostatic cancer in this series have been sufficiently encouraging to feel that in selected cases, especially in those showing a highly differentiated histological pattern, more adrenalectomies should be carried out in order that the place of the operation as a rational surgical procedure can be assessed.

I desire to thank my colleague, Mr. F. P. Raper, for permission to include in this series 2 cases of malignant prostate upon which he operated.

The treatment of these patients was carried out as part of an investigation sponsored by the Medical Research Council. I desire to thank the Medical Research Council for their help in supplying the cortisone.

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Mr. J. D. Fergusson: *Total Adrenalectomy for Malignant Disease of the Prostate and Breast.*

In 1952 some of us had the opportunity of seeing some of Professor Charles Huggins' patients in Chicago who had been treated by total adrenalectomy for advanced malignant disease of the prostate and breast. Being impressed with their progress I decided on our return to carry out adrenalectomy on some of my own reactivated cases of prostatic cancer. At the same time a parallel series of operations was to be performed on patients with metastasizing cancer of the breast.

A scheme was, therefore, drawn up for the selection of suitable cases and, through the generosity of the Medical Research Council, adequate supplies of cortisone for replacement therapy were made available to the Institute of Urology. This enabled us to make a start in November 1952, and I must here acknowledge my indebtedness to my surgical colleagues, Mr. T. G. I. James, Mr. H. G. Hanley and Mr. J. W. P. Gummer —and to my Research Assistant Mr. E. C. Gibson—with whose help I am now able to present details of 32 cases. Of these, 17 were patients suffering from prostatic cancer and 15 from cancer of the breast.

Selection of Cases

The selection of cases is a matter of considerable difficulty notwithstanding the inevitable outcome of the disease. It is assumed that only histologically proven cases will be chosen for which there is no alternative method of relief. With this proviso, the main considerations affecting the expediency of adrenalectomy are:

(i) The difficulty in distinguishing between tumours which remain hormone dependent and those which have become fully autonomous. (Theoretically, only the former should respond.)

(ii) The chance that any post-operative tumour response may be only temporary in nature.

(iii) The sustained liability to complications during the post-operative course—and the need for permanent substitution therapy.

(iv) The fact that patients suitable on theoretical grounds may be surgically unfit for other reasons.

(i and ii) On the first and second points, no certain estimate can be made in advance. It is reasonable to suppose, however, that some tumours which have previously responded to hormonal therapy will retain an element of dependence. Thus, following Huggins' advice, our cases of prostatic cancer have been chosen, as far as possible, from those showing a return of metastatic activity after earlier benefit from œstrogens or castration. We have not, as yet, used stimulating doses of ACTH to demonstrate residual androgen activity as a method of selection.

A majority of our breast cases have likewise shown a previous response to œstrogens or testosterone, and preference has been given to those in which histological examination has shown a well-differentiated tumour. In many cases vaginal smears have been examined pre- and post-operatively, but no conclusions have yet been reached on whether the absence of an œstrogenic response contra-indicates operation.

(iii) *Liability to complications.*—It must be stressed that full facilities for biochemical control should be available. Adrenalectomy implies much more than the mere removal of an androgen depot, and disturbances of electrolyte and water balance are only avoided by carefully controlled replacement therapy. The need for this extends throughout the period of survival since temporary Addisonian attacks have occurred in some of our patients several months after operation.

(iv) *Operability.*—Careful assessment of the cardiovascular condition and the metabolic state is required. Practical and theoretical considerations are often in conflict on the best time to operate, and whether the operation should be done in one or two stages; the general tendency being to defer

operation until the case is almost moribund. This doubtless accounts for the early post-operative mortality in some of our cases, but expediency has to be tempered with humanity. We have concluded that in the elderly prostatic cases only one adrenal should be removed at a time, the first operation to include castration. In breast cases a similar routine is advocated or, alternatively, bilateral adrenalectomy may be carried out as a one-stage procedure when oophorectomy has been undertaken earlier. Whether the operation is carried out in one or two stages, the final ablation of adrenal tissue must be accompanied by adequate replacement therapy. A suitable regime has been laid down by Huggins and Bergenstal (1951), but recent work in connexion with cortisone absorption has led us to suggest the following modifications:

Day		
OP. −2..	Cortisone acetate 200 mg. I.M. (divided doses)	Salt, 4 grams. (orally)
OP. −1..	Cortisone acetate 200 mg. I.M. with DOCA 5 mg. I.M.	,,
OP. 6 a.m.	Cortisone acetate 100 mg. orally.	
Noon	Cortisone acetate 50 mg. I.M., and thereafter six-hourly. DOCA 200 mg. implanted subcutaneously at operation.	
OP. +1	Cortisone acetate 50 mg. I.M. six-hourly.	
OP. +2	Cortisone acetate 50 mg. I.M. eight-hourly.	
OP. +3	Cortisone acetate 50 mg. orally eight-hourly.	
OP. +4	Cortisone acetate 25 mg. orally six-hourly.	
OP. +5	Cortisone acetate 25 mg. orally eight-hourly.	
Subsequently cortisone acetate 25 mg. usually twice a day.		

Daily measurement of fluid intake and output to avoid water retention.

Daily (early morning) estimation of serum Na, K, and fasting blood sugar.

Give fluids, blood, noradrenaline (Levophed), glucose and salt as necessary. Also thyroid extract grain ½ b.d. if required.

The effect of this is to build up an adequate reserve of cortisone before operation, while the DOCA implant gives greater security in maintaining the salt and water balance for a prolonged period. Reimplantation of DOCA is advisable after six months. Intramuscular cortisone gives way to cortisone by mouth on the third post-operative day, gradual reduction leading to a maintenance dose of approximately 50 mg. daily. This should be given in divided doses morning and evening. The addition of thyroid extract is said to enhance the effect of the cortisone and has certainly benefited one of our cases.

Clinical and biochemical observations would seem to indicate that the absorption of cortisone given by the oral route is not entirely regular. We have some reason to believe that the particulate size of different cortisone preparations shows a wide variation which may have a bearing on this point, and further research is at present proceeding.

Having prepared the patient in this way the surgical technique of adrenalectomy presents little difficulty to those familiar with approaching the kidney through the bed of the twelfth rib. The gland is, however, friable and its margins often ill-defined in the surrounding fat. Total removal is essential and this is best achieved by sweeping both gland and fat downwards from the undersurface of the diaphragm. This renders dissection much easier and allows early exposure of the adrenal vein. At one time, in an attempt to outline the contours of the gland in fat subjects, we resorted to intravenous injections of a dye (Kiton fast green) which was reported to stain all the body fat with the exception of the lipoids and the adrenal. This was certainly effective, but at the same time produced an embarrassing discoloration of the patient during the operation and for the next forty-eight hours.

Examination of the excised adrenal not infrequently shows the presence of a metastatic focus, slightly more common in our experience in cases of breast cancer than of prostatic cancer (breast 6, prostates 4). The total weights of the adrenals in our series, however, showed no significant increase over normal (in contradistinction to the findings of others).

Of the 32 cases which have been operated upon 17 were patients with metastasizing cancer of the prostate, the indications for adrenalectomy being severe metastatic pain in each instance. A majority were bedridden, and most had widespread skeletal deposits.

Fig. 1 indicates the pre-operative duration of the disease from the time of histological diagnosis (sustained hormonal therapy was given throughout this period), the staging of castration and adrenalectomy, and finally, the post-operative survival. 2 cases died within forty-eight hours of total adrenalectomy—one from carcinomatosis, the other from acute adrenal failure—and these were excluded from further consideration.

Fig. 2 shows similar details of 15 cases of cancer of the breast submitted to total adrenalectomy. 8 had previously received œstrogen or testosterone with varying benefit. Many of these cases exhibited widespread metastatic activity, the main clinical indications for operation being shown in Table I.

Two breast cases died within forty-eight hours of operation, from cardiac failure and carcinomatosis respectively. Both patients had commencing paraplegia, and they are excluded from further consideration.

Evaluation of all cases surviving the immediate post-operative period has followed the line previously adopted for œstrogen treatment for prostatic cancer, namely, assessment of the clinical response, the radiological behaviour of metastases, biochemical and serological variations; and, finally, histological changes in the tumour.

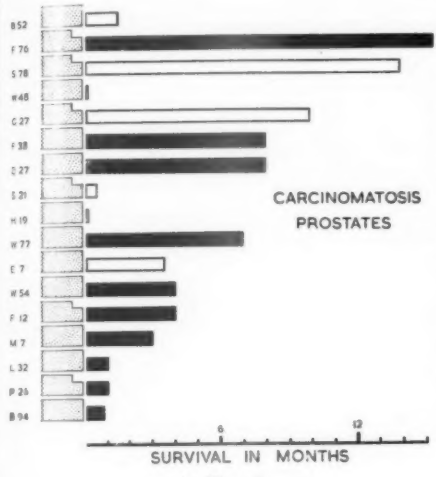


FIG. 1

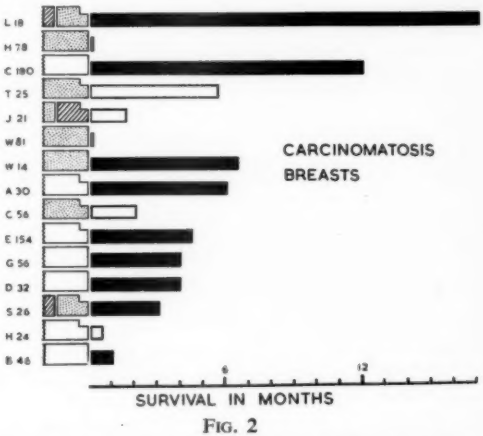


FIG. 2

FIGS. 1 and 2.—Total adrenalectomy for advanced cancer of the prostate (17 cases) and of the breast (15 cases). Figures in the left-hand margin denote (in months) the duration of the disease from the time of diagnosis. Stippled areas represent previous treatment with œstrogens. Hatched areas represent testosterone. All cases were castrated. Stepped edging indicates adrenalectomy in two stages. Horizontal columns give survival (in months) after total adrenalectomy: black = alive (18 out of 19 cases in good health); white = subsequently dying (in most cases after a response).

TABLE I.—CLINICAL INDICATIONS FOR TOTAL ADRENALECTOMY IN 32 CASES OF ADVANCED CANCER OF THE PROSTATE AND BREAST

ADRENALECTOMY FOR CANCER OF THE PROSTATE & BREAST.
INDICATIONS FOR OPERATION

PROSTATIC CANCER (17 CASES)

SKELETAL METASTASES 17 CASES

MAIN CLINICAL INDICATION FOR OPERATION PAIN (17 CASES)

BREAST CANCER (15 CASES)

CASE	PRIMARY TUMOUR	METASTASES BONE	METASTASES LUNG & PLEURA	METASTASES SKIN	MAIN CLINICAL INDICATION FOR OPERATION
1			+		DYSPNOEA (6 CASES)
2			+		
3			+		
4			+	+	
5			+	+	
6			+	+	
7		+			PAIN (3 CASES)
8		+		+	
9		+	+	+	
10		+			CACHEXIA (3 CASES, 2 WITH COMMENCING PARAPLEGIA)
11		+			
12		+		+	
13		+			PATHOLOGICAL FRACTURE (1 CASE)
14	+				FIXED FUNGATING PRIMARY TUMOUR (2 CASES)
15	+		+		

TABLE II.—SUMMARY OF RESULTS OF TOTAL ADRENALECTOMY IN 32 CASES OF ADVANCED CANCER OF THE PROSTATE AND BREAST

SUMMARY OF RESULTS OF ADRENALECTOMY IN CARCINOMATOSIS

PRIMARY ORGAN	TOTAL CASES	P.O. DEATHS	NO IMPROVEMENT	IMPROVEMENT	LONGEST SURVIVAL
BREASTS	15	2	3 (ALL DEAD)	10 (9 A. & W.)	17 MONTHS (A. & W.)
PROSTATES	17	2	3 (2 DEAD)	12 (9 A. & W.)	16 MONTHS (A. & W.)
WHOLE SERIES	32	4	6 (5 DEAD)	22 (18 A. & W.)	17 MONTHS (A. & W.)

OPERATIVE MORTALITY = 12·5 %

CLINICAL RESPONSE

Prostatic cancer.—Of 15 cases surviving operation all had remission of metastatic pain for periods ranging up to sixteen months. Of these 9 remain alive and well with sustained benefit. Of the 6 who died, temporary remission ranged from one week to thirteen months. General evidence of improvement, gain in weight and a return to ambulant activity occurred in all patients for a correspond-

ing period. Objectively, shrinkage of the primary growth (in some cases to imperceptible size) was a striking feature in the majority. This did not occur *pari passu* with regression of the metastatic lesions, and suggests the possibility of a different growth pattern for the primary and secondary tumours.

Breast cases.—Of 13 cases surviving operation the clinical improvement in patients with pulmonary lesions has perhaps been most satisfactory. 5 out of 6 patients with severe dyspnœa have had a remission and, so far, maintain their progress over periods ranging from one to eighteen months. Pre-operatively several had required confinement to bed in an elevated position to permit adequate ventilation. These have now all returned to ambulant activity.

2 of our 3 patients with metastatic pain had remission of five months or over—one remaining alive and well. The third case showed no response, dying two months later from carcinomatosis.

The one case of cachexia surviving operation was not benefited and died six weeks later.

One case with a pathological fracture is alive, with the fracture well healed, four months after operation.

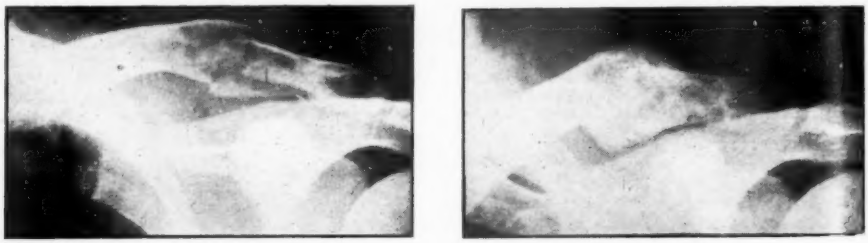
2 cases with fungating primary tumours are alive and well after three and six months respectively, both being back at work with complete healing of the lesion.

Similarly, in 6 patients with cutaneous nodules, marked or complete regression has been observed in all but 2.

In one case suffering from a "big arm" after radical mastectomy and X-ray therapy two years earlier, marked reduction of the swelling took place after adrenalectomy. We are, however, of the opinion that, in view of the time interval, this was due to the effect of cortisone on the fibrosis rather than an endocrine response on the part of the tumour.

Radiological response.—No significant change has been observed in the appearance of the sclerotic bone deposits in any of the prostatic cases. In one patient, however, who has so far survived for sixteen months an osteolytic secondary has recently appeared in the thoracic spine.

On the other hand, marked re-ossification has occurred at the site of pathological fracture in a breast case (Fig. 3).



A B

FIG. 3.—Re-ossification at the site of a pathological fracture of the clavicle after total adrenalectomy in a case of cancer of the breast. A, before operation, B two months later.

Even more striking are the changes noted in pulmonary metastases where complete regression has apparently taken place (Fig. 4).

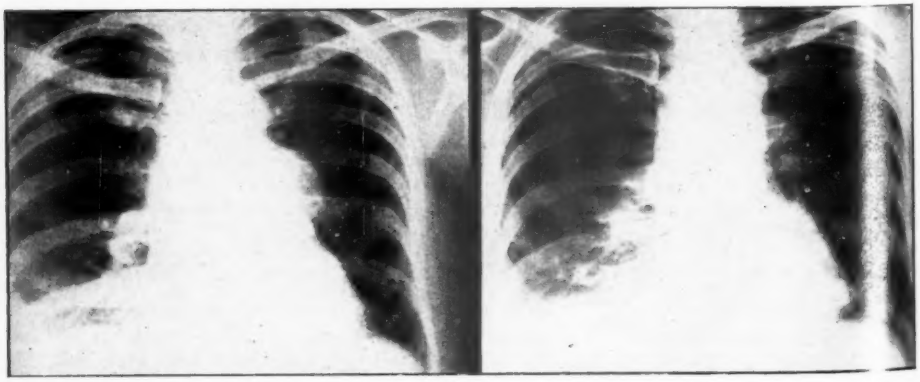


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FIG. 4.—Regression of pulmonary metastases in a case of cancer of the breast treated by total adrenalectomy. A, before, and B, three months after, operation.

Biochemical and serological response.—The expected fall in androgen production, following adrenalectomy, cannot be assessed by routine methods of estimating the urinary ketosteroids. With these at present, no adequate distinction can be made between 17-ketosteroids and certain end-products of cortisone metabolism.

Biochemical study is, therefore, mainly concerned with the estimation of the serum acid and alkaline phosphatase in prostatic cases, and with calcium excretion in breast cancer with bone secondaries.

Prior to adrenalectomy, during the stage of tumour reactivation, a rise of alkaline phosphatase generally preceded an increase of the acid enzyme, and this may furnish a guide as to the time to operate. Post-operatively both acid and alkaline enzymes fall abruptly.

In breast cases we have made a limited study of the urinary calcium loss in cases with widespread osteolytic metastases. Fig. 5 shows a negative balance before operation and a return to normal after adrenalectomy. It is of interest to note that a partial restoration of balance occurred after removal of the first adrenal and before cortisone was given. This would indicate that a measure of tumour control had already been achieved which could not be ascribed to cortisone.

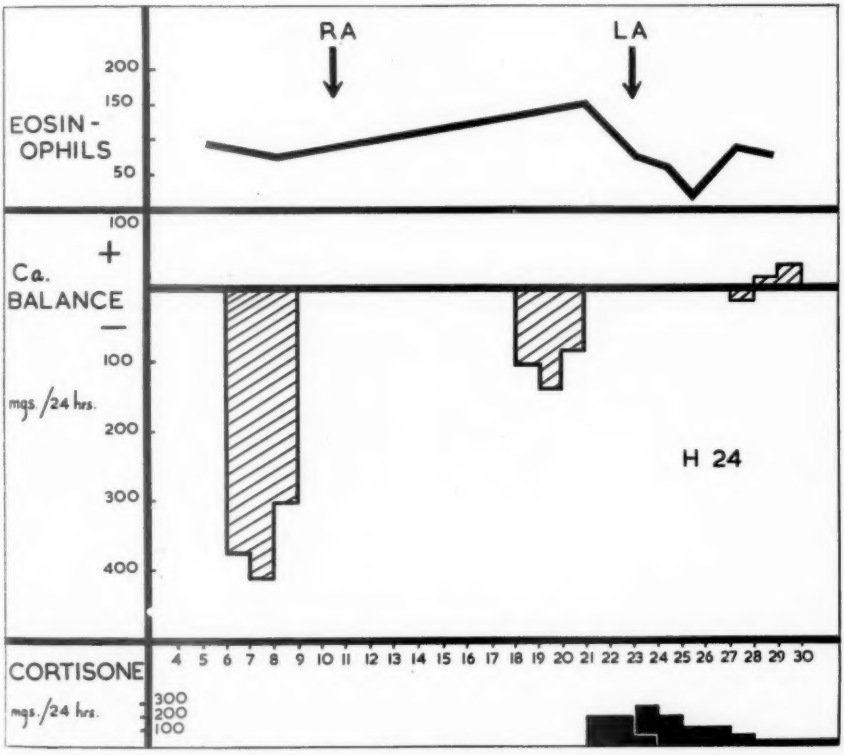


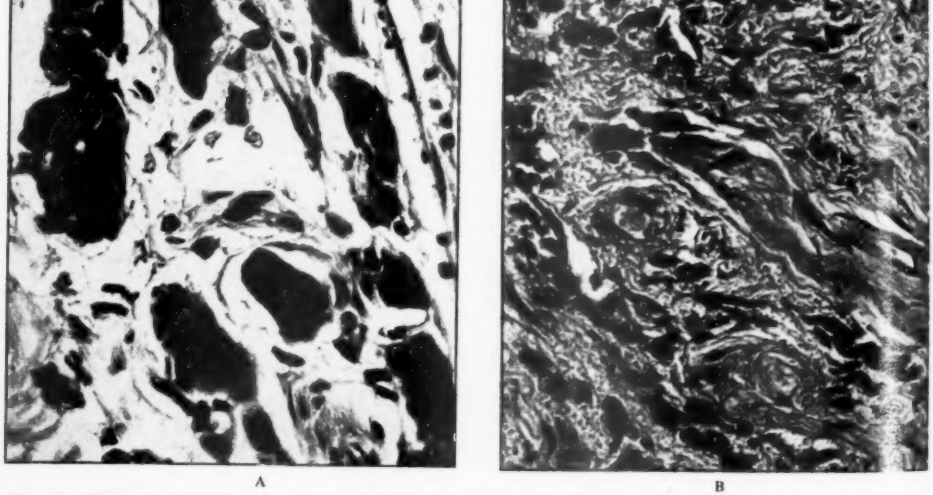
FIG. 5.—Urinary calcium excretion in a case (H.24) of cancer of the breast with widespread osteolytic metastases. Arrows indicate times of right and left adrenalectomy. Note the decrease in calcium loss after removal of the right adrenal (i.e. before cortisone is given) and restoration of normal balance following total adrenalectomy.

Repeated eosinophil counts as shown in this case are carried out routinely to assess the effectiveness of cortisone substitution.

Histological response.—From the scientific standpoint the beneficial effect of adrenalectomy should be capable of confirmation by histological methods. Unfortunately, suitable material is scarce. There is seldom any need for interference with cases which are responding well and, in those which die, the tumour may have become reactivated or autonomous. Two cases in our series have furnished microscopical evidence of regression. In the first, previously described by Franks (1953), the prostatic growth and its metastases showed massive necrosis six weeks after adrenalectomy (Fig. 6). In the

second case, repeated biopsies of skin nodules in a patient with breast cancer demonstrated a gross reduction of tumour activity (Fig. 7).

FIG. 6.—Transverse section through the prostate and rectum showing massive necrosis of the former in a post-mortem specimen six weeks after total adrenalectomy for prostatic cancer. (Reproduced by kind permission of the *British Medical Journal*, Franks, L. M. (1953) Fig. 1, Plate II.)



A B

FIG. 7.—Photomicrographs (× 1160) of sections through two similar secondary skin nodules from a case of cancer of the breast treated by total adrenalectomy. A, before, and B, after operation.

The evidence afforded by repeated examination of vaginal smears for œstrogenic activity before and after adrenalectomy has, so far, been equivocal.

Having considered examples of tumour response it remains to be decided how far this may be ascribed to adrenalectomy, or whether the preceding gonadectomy or substituting cortisone is responsible. With regard to the former, the interval between castration and adrenalectomy has been sufficiently long in many published cases (and in several of our own) to leave no doubt that a further

phase of hormone control can be attained. This has not been so clearly established in breast cases, where oophorectomy has generally been undertaken at the time of adrenal ablation.

The possibility that cortisone therapy, rather than adrenalectomy, is responsible for any improvement must still remain under review. However, in one of the cases quoted earlier partial restoration of the calcium balance took place after unilateral adrenalectomy before any cortisone was given. We have also observed a small series of controls using cortisone treatment alone without operation; in these, apart from occasional symptomatic improvement, there has been no objective evidence of tumour response.

Disregarding the actual mechanism of tumour control we can at least summarize our results in the present series as shown in Table II.

Firstly, bilateral adrenalectomy can be carried out on cases of advanced metastasizing cancer at a not unreasonable risk compared with the gravity of the condition (4 post-operative deaths in 32 cases). Secondly, adrenalectomized patients can be maintained in an adequate state of metabolic balance for prolonged periods by oral substitution therapy. Thirdly, although post-operative tumour response cannot be ensured, the method of selection adopted here has yielded a high proportion of remissions. Thus roughly three-quarters of our patients have obtained relief of symptoms, combined in most cases with evidence of tumour regression. Many of these patients remain in good health and have returned to normal activity over periods extending up to seventeen months. The period of review is still too short to justify final conclusions.

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Mr. Howard G. Hanley: *Bilateral Total Adrenalectomy for Malignant Hypertension*

The mechanism whereby the blood pressure is maintained at a relatively constant level is incompletely understood, while the causes of hypertension are even more debatable. During recent years, certain facts have emerged which show some relationship at least between the adrenal cortex and hypertension. For example, if a hypertensive patient develops Addison's disease the blood pressure becomes normal or lowered, while if such a patient is then given desoxycorticosterone in *ample* dosage, hypertension recurs.

Secondly, the benefit of a salt-free diet in hypertension has long been recognized, while the sodium-retaining effects of desoxycorticosterone are now well known.

It is not assumed that some dysfunction of the adrenal gland itself is the cause of malignant hypertension, but by performing a total adrenalectomy it should be possible to eliminate the salt-retaining steroids which are presumed to be hypertensive factors. If a suitable replacement therapy for each individual can then be worked out, it should be possible to control the salt and water retention so that a reasonably active existence is possible. This is one theory behind the principle of adrenalectomy for malignant hypertension.

The treatment of hypertension by subtotal adrenalectomy was originally carried out by DeCourcy (1950) in the late 'twenties and the early 'thirties, when he found that if too much gland tissue was removed, the mortality was high, while if too much was left in situ the effect on the hypertension was negligible. This was a fundamental observation. The blood pressure could be reduced in all cases provided enough adrenal tissue was removed, but since adequate substitution therapy was not then available, the surgeon naturally erred on the side of removing too little rather than too much, with the result that in most cases little change resulted from the operation.

However, the problem was not only concerned with estimating the size of the piece to be removed since each patient reacts differently. Nine years ago I performed a unilateral subtotal adrenalectomy on two hypertensive patients with immediate moderate reduction of blood pressure in both of them, but in one case the hypertension had returned within three months. Seven years ago in another patient, I removed all of one gland and three-quarters of the other—without any effect on the hypertension at all, in spite of the fact that this was a much more radical excision than in the previous 2 cases. Quite obviously, insufficient adrenal tissue had been removed in all of these patients.

In more recent years, surgeons have become bolder, and in 1950 DeCourcy reviewed his most recent 30 cases in which some four-fifths of each gland was removed in two stages with an interval of three months. 75% of his patients showed a significant fall in blood pressure, while a few returned to normal, some for as long as twelve years.

Zintel *et al.* (1951) reviewed 26 cases of subtotal adrenalectomy associated on occasion with sympathectomy. In 1953 Bowers *et al.* described 23 patients in which they left behind a small piece of adrenal, which they described as "about the size of the thumb nail" on the one side and at a second stage removed the whole of the gland on the other side. In this series the blood pressure failed to return to normal in only one case, and this patient died approximately two months later. There is therefore no doubt that, if sufficient adrenal tissue is removed, the blood pressure can be lowered, even in the most severe hypertensive states, but if too much gland is left in situ the operation will prove disappointing.

TOTAL ADRENALECTOMY

With the development of really effective replacement therapy using cortisone, the danger of removing too much adrenal tissue has been overcome. In 1952 Hartwell Harrison and his colleagues published

their preliminary report on bilateral total adrenalectomy for malignant hypertension. Some of their cases were *in extremis* before operation, but even then, 9 out of 14 survived operation and showed definite subjective and objective improvement, while really significant falls in blood pressure occurred in 4 cases.

In my own series of bilateral adrenalectomy cases for carcinoma of prostate and breast, there were 5 patients with marked hypertension before operation. The pressure is now much reduced in all of them, the degree of reduction appearing to depend upon the dosage of cortisone required to maintain their well-being.

One prostatic cancer case is particularly interesting. He accepted his bilateral adrenalectomy only too willingly in the hope of relieving his severe backache and sciatic type pains. The fact that his blood pressure was 190/125, and that he had cardiac dilatation with œdema of the legs and shortness of breath, were relatively unimportant findings, and were attributed to his prostate. After operation the back pains were, of course, relieved, and taken for granted, but the thing which now impresses the patient most of all is his ability to walk up and down stairs, and even use his wheelbarrow in the garden. This is certainly due to the fact that his blood pressure is now only 140/85, and his cardiac congestion is relieved. These 5 cases were, of course, not malignant hypertensives and one would not suggest performing adrenalectomy operations on such patients in the absence of any other indication.

The problem of *true malignant hypertension* is, however, quite different. Medical treatment has failed them, while sympathectomy offers little hope in such advanced cases. My own experience of total adrenalectomy for malignant hypertension *per se* is small, and limited to 5 patients. These had all reached the stage where my medical colleagues advised me that there was nothing to lose by taking the risk of such an operation.

Case I was a woman of 46 with gross eye changes and severe cardiac failure. She had been a patient of mine some fifteen years previously with a severe pyelonephritis of pregnancy and we had watched the pyelonephritis progress throughout the years. At operation she showed marked respiratory embarrassment when placed upon her side and was altogether a very unpleasant anæsthetic and operative risk. However, her improvement after operation was quite dramatic, and this has been maintained for over a year. Her eye changes have cleared, her cardiac failure has disappeared and she has been looking after a busy household single-handed, including the shopping and the washing. Symptomatically she is cured, though her blood pressure is still raised above normal, but this is no bad thing in an ateriosclerotic patient.

Case II was a young woman of 30 who had a premature delivery with toxæmia six years ago. The fact that she was a hypertensive patient does not appear to have been detected until her next pregnancy two years later, and this had to be interrupted. Seven months ago she became pregnant again, aborted spontaneously and developed malignant hypertension. She was practically blind. Her urea clearance was only 45% of normal and her diastolic pressure was around 140 mm.Hg. A bilateral total adrenalectomy was performed, and now, six months later, she is able to look after her family and lead a normal life. Her vision is restored; the urea clearance is 80% of normal and her blood pressure is approximately 160/100, which is lower than it has been for six years as far as we know.

3 other cases of malignant hypertension have been similarly treated during the past month or so. Although less dramatic, they have been equally satisfactory so far. Here, then are 5 malignant hypertensive patients treated by total adrenalectomy without a death, and, in my opinion, this procedure is well worthy of further investigation and trial. At present it should be reserved for cases of established malignant hypertension, certainly until more information is available. Severe cardiac failure, and extensive eye changes do not preclude operation, but renal failure is a definite contra-indication. Hartwell Harrison states that a blood urea of 50 mg.% is the upper limit of safety. My first patient was above this level, but even so 50 mg.% is probably a useful level to work to.

The success of the operation should not be gauged only by the subsequent blood pressure level, because too great a fall of pressure in an arteriosclerotic patient would probably prove fatal. Of greater importance is the restoration of circulatory efficiency, as shown by a reduction in the heart size, the abolition of pulmonary congestion and peripheral œdema, together with the relief of headaches and the clearing of the eye changes.

The long-term follow-up of these patients will be all important. If the progressive vascular changes can be halted or slowed down, there may be a place for the operation in earlier, less severe cases, in an attempt to prevent the onset of arteriosclerosis.

As a genito-urinary surgeon my chief concern should be with cases of carcinoma of the prostate and breast, but I cannot help feeling that the restoration of a hypertensive middle-aged man or woman into the bosom of the family in an active capacity, is a greater economic service to the community than the temporary prolongation of the life of an old man of 80 years. However, on occasion total adrenalectomy would apparently do either.

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